

I U C L I D

Data Set

Existing Chemical : ID: 121-73-3
CAS No. : 121-73-3
EINECS Name : 1-chloro-3-nitrobenzene
EINECS No. : 204-496-1
TSCA Name : Benzene, 1-chloro-3-nitro-
Molecular Formula : C6H4ClNO2

Producer Related Part
Company : Solutia Inc.
Creation date : 04.04.2002

Substance Related Part
Company : Solutia Inc.
Creation date : 04.04.2002

Memo :

Printing date : 09.12.2002
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Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

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1. General Information

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2.1 MELTING POINT

Value : 46 - °C
Sublimation :
Method : other
Year : 1995
GLP : no
Test substance : other TS
Method : experimental, method not reported.
Test substance : m-Chloronitrobenzene
Reliability : (2) valid with restrictions
Also cited in reference document, Budavari, S. (ed). The Merck Index-an encyclopedia of chemicals, drugs and biologicals. Whitehouse Station, NJ. 1989. Cited as a Peer reviewed reference in HSDB (2002) for m-NCB.
Flag : Critical study for SIDS endpoint
06.12.2002 (9)

2.2 BOILING POINT

Value : 236 - °C at 1013.25 hPa
Decomposition :
Method : other
Year :
GLP : no data
Test substance : other TS
Method : Not reported
Remark : Reported as 236 deg. C @ 760 mm Hg.
Reliability : (2) valid with restrictions
Accepted reference standard and cited as a Peer reviewed reference in HSDB (2002) for m-NCB.
Flag : Critical study for SIDS endpoint
02.12.2002 (2)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : - .129 hPa at 25° C
Decomposition :
Method : other (measured)
Year : 1994
GLP : no data
Test substance : other TS
Method : Not reported
Test substance : m-Chloronitrobenzene
Reliability : (2) valid with restrictions
Original article cited as a Peer reviewed reference in HSDB (2002) for m-NCB.
Flag : Critical study for SIDS endpoint
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2.5 PARTITION COEFFICIENT

Log pow	:	= 2.49 - at 25° C	
Method	:	OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"	
Year	:	1987	
GLP	:	no data	
Test substance	:	other TS	
Method	:	Shake flask method; the experiments were conducted in triplicate. The test temperature was 25 +/- 0.5 deg. C. The concentration of the test substance in the aqueous phase was determined by UV/Visible Spectrophotometry, while the concentration in the n-octanol phase was calculated as the difference from the total amount added.	
Test substance	:	m-Chloronitrobenzene with purity > 99% from Aldrich Chemical Co.	
Reliability	:	(1) valid without restriction Conducted according to OECD guidance.	
Flag	:	Critical study for SIDS endpoint	
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2.6.1 WATER SOLUBILITY

Value	:	= 255.5 - mg/l at 25 ° C	
Qualitative	:	moderately soluble (100-1000 mg/L)	
Pka	:	at 25 ° C	
PH	:	- at and ° C	
Method	:	other	
Year	:	1995	
GLP	:	no	
Test substance	:	other TS	
Method	:	Group contribution methods allow for the estimation of water solubility based on the chemical structure of a given compound. Values assigned to substructural units (referred to as "fragments") are summed to give a final solubility for the entire compound. The fragment values used in this method were compiled from the KWB1 (Klopman, Wang and Balthasar, 1992, J. Chem. Inf. Comput Sci. 32:474-482) and WYMW (Wakita, KM, Yoshimoto, S Miyamoto and H Watanabe. 1986, Chem. Pharm. Bull 34:4663-4681) group contribution methods. Additionally, as this method traditionally models liquids better than solids, a melting point term was included to improve the values generated for compounds considered solids (i.e. melting point >25 deg C).	
Result	:	The estimated water solubility (Sw) of m-chloronitrobenzene was reported as log Sw[mol/l]= -2.79. Based on a molecular weight of 157.56 g/mol, the Sw=255.5 mg/l.	
Reliability	:	(2) valid with restrictions	
Flag	:	Critical study for SIDS endpoint	
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2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

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2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

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3.1.1 PHOTODEGRADATION

Type	: other
Light source	: Xenon lamp
Light spect.	: - nm
Rel. intensity	: - based on Intensity of Sunlight
Direct photolysis	
Half-life t _{1/2}	: -
Degradation	: - 98 % after 5 hour(s)
Quantum yield	:
Deg. Product	: yes
Method	: other (measured)
Year	: 1979
GLP	: no data
Test substance	: other TS
Method	: One ml of m-chloronitrobenzene in n-hexane was put in 1 L reaction vessel, followed by substitution of n-hexane vapor with air or nitrogen free from nitrogen oxides. The TS deposited in the reaction vessel which corresponded to 1000 microliter gas if vaporized, was irradiated at 25 to 30 degrees C for five hours with the Xenon lamp (ozone-less type, Ushio, Co.). Disappearance of parent TS measured by HPLC; by-products measured by GC-MASS.
Result	: Rate of disappearance was influenced by the intensity of light passing through either of two reaction vessels used in this experiment, i.e. pyrex and quartz. The rate of disappearance of MNCB in air free of nitrogen, when tested in pyrex and quartz vessels, respectively, was 3.6% and 89%. When MNCB was tested in nitrogen free of nitrogen oxides in pyrex and quartz vessels, respectively, disappearance rates were 8.9% and 98%. Reaction byproducts found in nitrogen-free air included: 3-chloro-2-nitrophenol, 3-chloro-6-nitrophenol and 3-chloro-4-nitrophenol. The reaction by-product in nitrogen free from nitrogen oxides was m-chlorophenol.
Test substance	: Laboratory synthesized, purity unstated.
Reliability	: (2) valid with restrictions Established photodegradative properties experimentally in published literature article.
Flag	: Critical study for SIDS endpoint
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Type	: other
Light source	:
Light spect.	: - nm
Rel. intensity	: - based on Intensity of Sunlight
Deg. Product	:
Method	: other (calculated)
Year	: 2002
GLP	: no
Test substance	:
Method	: Used AOP method in EPIWIN, 2002.
Result	: Vapor phase m-chloronitrobenzene is susceptible to reaction with photochemically-produced hydroxyl (OH) radicals. The 2nd order rate constant for reaction with hydroxyl radicals was calculated as 0.1199E-12 cm ³ /molecule*sec). Based on 1.5E6 OH molecules/cm ³ and assuming 12 hours of sunlight per day, the estimated photo-oxidation half-life is 89.2 days (~2140 hrs).
Reliability	: (2) valid with restrictions Supplemental information as a measured value has been used to fulfill this HPV Endpoint. Use of estimation model recommended by US EPA.
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3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	: fugacity model level III
Media	: other
Air (level I)	: 7.96
Water (level I)	: 28.8
Soil (level I)	: 63
Biota (level II / III)	:
Soil (level II / III)	: .193
Method	: other
Year	: 2002
Method	: Level III Fugacity Model; EPIWIN, Version 3.10. Physical properties of m-chloronitrobenzene used as model input: water solubility=255.5 mg/L, vapor pressure=0.097 mm Hg, log Kow=2.46 and melting point=44.4 deg C. Emissions rates were 1000 kg/hr for each of the three main compartments, air, water and soil. Also estimated sediment compartment, listed in second soil entry. Persistence Time: 550 hr.
Reliability	: (2) valid with restrictions Estimated values based on model recommended by US EPA.
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3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	: anaerobic
Inoculum	: anaerobic bacteria
Concentration	: 4µmol/l related to Test substance related to
Contact time	: 1 year
Degradation	: 50 - % after 3.2 day
Result	:
Deg. Product	: yes
Method	: other
Year	: 1996
GLP	: no data
Test substance	: other TS
Method	: This study was conducted to examine degradation of chloronitro compounds in sulfidogenic anaerobic sediment. A 2.0 x 10E-3 M stock solution of the test substance was prepared in methanol. The test medium was a slurry of estuarine sediment and river water from the mouth of the Tsunumi river (Japan). Initial characteristics of the medium were: solids,

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	<p>Tsunami river (Japan). Initial characteristics of the medium were: solids, 272 +/- 2.8 g/kg; nitrate, not detected (sediment), and 4 mg/l (water); sodium chloride, 1.7% (sediment) and 1.5% (water); sulfate, 1980 mg/l (sediment) and 1840 mg/l (water); pH of 5.6. Tests were conducted in screw-top test tubes. Twenty-five (25) tubes containing 5 ml test medium were prepared under nitrogen and stored for 1 week at room temperature to allow the test system to become anaerobic. Eight (8) tubes were autoclaved for use as sterile controls. Five (5) tubes were prepared with filtered river water only as the test medium, for use as sediment-free controls. Ten (10) ul of the stock solution was added to each tube yielding an initial concentration of 4 umole/l. All tubes were placed in an anaerobic chamber (10% H₂, 10% CO₂, 80% N₂) at 25 deg. C. Test tubes were hand-mixed 3 times per week by inverting and were sampled for analysis at the beginning of incubation (t=0 hrs) and at various time intervals over the course of the test period (1 yr). Collected samples were frozen. The experiment was conducted in duplicate. Measurement of remaining test substance and identification of degradation products were conducted at the end of the test period using gas chromatography with mass-selective detection (GC-MS). Measured concentrations at each time interval were compared to measured concentrations at t=0 hrs. The first order rate constant (k) was determined by linear regression. The characteristic half-life (t_{1/2}) was determined by the equation $t_{1/2} = (\ln 2)/k$.</p>
Result	: Degradation of the parent compound was observed to occur without any lag time. The first order rate constant (k) was determined to be 0.216 +/- 0.096 per day. The half-life was determined to be 3.2 days. The coefficient of determination was reported as 0.89. Under the conditions of the test and in the presence of the sediment used, m-NCB was observed to degrade under anaerobic conditions in a two-stage process: (1) reduction of the nitro substituent group to form 3-chloroaniline and (2) removal of the chloro-substituent group to form aniline.
Test substance	: commercial grade mNCB from Tokyo Kasei Kogyo Col. Ltd, Japan; purity not specified but likely >99%.
Reliability	: (2) valid with restrictions Non standard test system, but well documented; individual data for test substance recoveries not provided.
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Type	:
Inoculum	: aerobic microorganisms
Concentration	: 10mg/l related to Test substance related to
Contact time	: 64 day
Degradation	: - % after
Result	:
Deg. Product	: not measured
Method	: other
Year	: 1961
GLP	: no
Test substance	: other TS
Method	: The study was conducted to examine the effect of substituent groups on the potential degradation of benzene compounds by soil microorganisms. The test medium was a mixture of distilled water (1000 ml), K ₂ HPO ₄ (1.6 g), KH ₂ PO ₄ (0.4 g), NH ₄ HO ₃ (0.5g), MgSO ₄ .7H ₂ O (0.2 g), CaCl ₂ .2H ₂ O (0.025 g), and FeCl ₃ .6H ₂ O (0.0023 g). The inoculum was a 1 % suspension of Niagara silt loam. Tests were conducted in 4 oz screw-cap bottles (45 m diameter x 80 mm high). The test substance (final substrate concentration = 10 mg/l), 40 ml of test medium, and 1 ml of inoculum were combined in a test vessel and incubated at 25 deg C in the dark. An unspiked control mixture (medium + inoculum) was prepared and incubated concurrently. Test vessels were prepared in duplicate. Two additional series of vessels were prepared to evaluate (a) the effect of HgCl ₂ (8 mg) + Tween-80 (5.03-7) on degradation, and (b) the potential

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	<p>HgCl₂ (8 mg) + Tween-80 (5.03-7) on degradation, and (b) the potential toxicity of the test substance to the inoculum. The toxicity control contained glucose (1%) + test substance. Test vessels were mixed and sampled for analysis at 3 and 6 hrs, and at 2, 4, 8, 16, 32, and 64 days after test initiation. Analyses were conducted using a UV spectrophotometer. Solutions containing the test substance were compared against the untreated control and degradation (given as cleavage of the benzene ring) would be demonstrated by a loss of UV absorbency.</p>
Result	<p>: The wavelength reported for measuring the degradation of 3-chloronitrobenzene was 265 nm. Degradation of the test substance, i.e. breakdown of the benzene ring, was observed to be difficult and did not completely occur during the test period. Under the conditions of the test, degradation of the monochloronitro group of compounds by soil microorganisms, was reported to be > 64 days. Additionally, HgCl₂ did not appear to affect the degradation rate of the test substance, and the test substance did not appear to be toxic (i.e. after the rate of microbial development) to the inoculum.</p>
Test substance	<p>: m-NCB, purity unspecified.</p>
Reliability	<p>: (2) valid with restrictions Provided as Supplementary information for this HPV Endpoint; study was non-standard and predated GLPs, but was well documented.</p>
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3.6 BOD₅, COD OR BOD₅/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: flow through
Species	: Pimephales promelas (Fish, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: yes
LC50	: = 18.8 -
Method	: other
Year	: 1986
GLP	: no data
Test substance	: other TS
Method	: US EPA methodology (unspecified which one); Fathead minnows used in the tests were cultured from brood stock provided by the USEPA Environ. Res. Lab (Duluth) and the University of Wisconsin-Superior. Fish used were 33 days old and had a calculated mean weight of 0.148 g. Fish were not fed during the test. The toxicity test was conducted using 19-L vessels. Test volume was 7.3 L. The control/dilution was unfiltered Lake Superior water. Water quality parameters measured during the test included: total hardness, 45.3 +/- 0.58 mg/l (as CaCO ₃); alkalinity, 42.8 +/- 0.45 mg/l (as CaCO ₃), dissolved oxygen, 7.0 +/- 0.21 mg/l, temperature, 23 +/- 0.11 deg. C., and pH, 7.45 +/- 0.06. Test concentrations were analyzed daily (single sample; alternating replicates) by GLC. Two replicates of 25 fish each were exposed to the control/dilution water and to each of five measured concentrations of the test substance. Mortality and abnormal signs of behavior were recorded at 3, 6, 24, 48, 72 and 96 hrs. LC50 tabulated using the Trimmed Spearman-Kärber method.
Result	: Average measured concentrations (test replicate): control= <0.25 mg/L (limit of detection), Dosage # 1 - 3.15 mg/l (replicate 1) and 2.8 mg/l (replicate 2), Dosage # 2 - 5.05/4.5 mg/l; Dosage # 3 - 7.25/10.0 mg/l; Dosage # 4 - 14.4/12.9 mg/l; Dosage # 5 - 24.1/22.4 mg/l. The concentration of test material was maintained during the exposure period (percent recovery was reported as 95.6 +/- 1.9 %). Results of the 96 hr acute toxicity test by concentration: No deaths at 0 or Dosages 1-4; at Dosage # 5 partial mortality was observed between 3-6 hr after treatment. 100 % mortality was seen in replicate 1 @ 24 hr while 92 % mortality was seen in replicate 2 at 24 hrs. No further deaths were observed later in the study period. The 96-h LC50 was reported as 18.8 mg/L. Affected fish were reportedly hypoactive, lost schooling behavior and lost equilibrium prior to death.
Test substance	: m-CNB from Aldrich Chem. Co. with purity of 98%.
Reliability	: (2) valid with restrictions Well documented study conducted under EPA test guidelines; no EC50 determined, nor were CI measured (unreliable by stat. method used)
Flag	: Critical study for SIDS endpoint
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Type	:
Species	: other
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no
LC50	: = 43.2 -
Method	: other
Year	: 2002
GLP	: no
Test substance	: no data
Method	: calculated using ECOSAR.
Result	: An acute fish 96-h LC50 was calculated using ECOSAR from US EPA; the

SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.

Reliability : (2) valid with restrictions
Provided as Supplementary information; model used has been accepted by US EPA.

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4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring :
EC50 : c = 47.7 -
Method : other
Year : 2002
GLP : no
Test substance : no data
Method : An acute Daphnia 48-h LC50 was calculated using ECOSAR. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.

Reliability : (2) valid with restrictions Estimate obtained from US EPA recommended model and supported by additional literature data included in this section.
Estimate obtained from US EPA recommended model and supported by additional literature data included in this section.

Flag : Critical study for SIDS endpoint

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Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no data
EC50 : = 20 -
Method : other
Year : 1980
GLP : no data
Test substance : other TS
Method : NEN 6501 -"Determination of acute toxicity with Daphnia magna". Dutch Standardization Organization, Rijswijk, The Netherlands. The 48-h acute test was conducted with three CNB isomers. The LC50 and 95% confidence limits were determined by the Litchfield and Wilcoxon (1949) method.

Result : LC50=20 mg/l with CI of 10-32 mg/L. Relative toxicity of the three CNB isomers were (high to low): para>meta>ortho.

Test substance : m-NCB purity of 99%, obtained from Merck.

Reliability : (4) not assignable Provided as Supplemental data, in that study, as published, provides insufficient individual data to allow higher categorization.
Provided as Supplemental data, in that study, as published, provides insufficient individual data to allow higher categorization.

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4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	: other algae	
Endpoint	:	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
Analytical monitoring	:	
EC50	: c = 30.6 -	
Method	: other	
Year	: 2002	
GLP	: no	
Test substance	:	
Method	: Method of calculation of an acute green algal 96-h LC50 used ECOSAR from USEPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.	
Reliability	: (2) valid with restrictions Estimate obtained from US EPA recommended model and supported by additional literature data included in this section.	
Flag	: Critical study for SIDS endpoint	
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Species	: Chlorella pyrenoidosa (Algae)	
Endpoint	: other	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
Analytical monitoring	: no data	
EC50	: = 1.9 -	
Method	: OECD Guide-line 201 "Algae, Growth Inhibition Test"	
Year	: 1984	
GLP	: no data	
Test substance	: other TS	
Method	: The 96-h EC50 for effects on yield and 95% confidence limits were determined by the method of Kooyman et al, 1983 and followed guidance of OECD # 201. Yield was the point of measurement.	
Result	: The 96-h EC50=1.9 mg/l with confidence limits of 1.5-2.6 mg/l.	
Test substance	: m-NCB with purity of 99% obtained from Merck.	
Reliability	: (4) not as signale Provided as Supplemental data, in that study, as published, provides insufficient individual data to allow higher categorization.	
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4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

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4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: rat
Strain	: Sprague-Dawley
Sex	: male/female
Number of animals	: 50
Vehicle	:
Value	: = 400 - mg/kg bw
Method	: OECD Guide-line 401 "Acute Oral Toxicity"
Year	: 1983
GLP	: yes
Test substance	: other TS
Method	: Used 5 rats per sex per each of 6 dose groups: 0, 200, 251, 316, 398, and 501 mg/kg; test article was administered undiluted once via gavage and animals observed for up to 14 days. Daily observations were made for mortality and clinical signs of toxicity. Body weights were recorded prior to start of the study and weekly thereafter. Necropsies were performed on all animals. Food and water were given ad libitum and humidity and temperature controlled. LD50 and 95% CI calculated according to method of deBeer, 1945, J. Pharmacol. Experimen. Ther. 85:1.
Result	: Oral LD50 calculated as 400 (95% Confidence Limits of 350-470) mg/kg. Deaths occurring at each dose level included: At 200 mg/kg - 0/5M, 0/5F; at 251 mg/kg-2/5M, 0/5F, at 316 mg/kg-1/5M, 2/5F, at 398 mg/kg-5/5M, 0/5F, at 501 mg/kg-5/5M, 5/5F. Deaths occurred almost universally within the first 24 hr of dosing. Generalized signs of toxicity included lethargy, weakness and collapse before death. No other overt signs of toxicity were seen. At necropsy of decedents the following observations were made: hemorrhagic lungs, discoloration of the liver, kidney and spleen (2 cases) and gastrointestinal irritation. No discernable observations were noted for survivors necropsied after 14 days on test.
Test substance	: Purity of 98%.
Reliability	: (1) valid without restriction Meets OECD guidance and conducted under GLPs
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5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	: rat
Sex	: no data
Strain	: other
Route of admin.	: oral unspecified
Exposure period	: up to 7 months
Frequency of treatment	: daily
Post obs. period	:
Doses	: 60 mg/kg for 20 days; 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months
Control group	: yes
NOAEL	: = .005 - mg/kg bw
Method	: other
Year	: 1967
GLP	: no data
Test substance	: no data
Method	: Peroral treatment of 20 albino rats at 60 mg/kg for 20 days, followed by peroral administration of MNCB to groups of rats at 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months. Measured indices reportedly included hematology, liver function (blood and urine) and peripheral blood pathology.
Result	: 4/20 rats treated with 60 mg/kg MNCB for 20 days died. Groups of rats treated for 7 months exhibited marked changes in peripheral blood. Methemoglobin levels were increased within the first month of testing in the HD group; elevations occurred in groups treated with 0.025 mg/kg MNCB or higher. Hemoglobin was reduced and reticulocytes, serum alkaline phosphate and urinary bilirubin were elevated along with presence of Heinz bodies in erythrocytes at dosages of 0.025 mg/kg/d and above. The NOEL was 0.005 mg/kg/d.
Conclusion	: Comparative study using ONCB, MNCB and PNCB. Concluded that PNCB was the most toxic isomer following systemic exposure, MNCB was intermediate, and ONCB was the least systemically toxic of the three isomers tested. All isomers exhibited essentially the same pattern of toxicity.
Reliability	: (4) not assignable Supplemental information, as this report provides but a summary of results without sufficient detail to be classified higher.

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5.5 GENETIC TOXICITY 'IN VITRO'

Type	: Ames test
System of testing	: S. typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538
Concentration	: 25.6, 51.2, 102.4, 204.8, 409.6, 819.2, 1638.4 and 3276.8 ug/plate
Cycotoxic conc.	: 3276.8 ug/plate
Metabolic activation	: with and without
Result	: negative
Method	: other
Year	: 1977
GLP	: no
Test substance	: other TS
Method	: Design consistent with but preceded OECD Testing and GLP guidance. Tester strains obtained from B. Ames, S9 fraction came from PCB injected male SD rats, test article dissolved in DMSO for use in pour-plate method for quantitative determination of mutagenic activity according to Ames. A negative control group used 0.05 ml DMSO while positive controls tested were: MNNG, 2-NF, 9-AA and 2-AA (S9 added only). All tests were performed in duplicate and repeated at least three times. A positive response was identified when colonies of his+ revertants on test article-

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	response was identified when colonies of his+ revertants on test article-treated plates were more than twice the number of revertant colonies on the control plates.	
Result	: No 2X mutagenic response was observed at any treatment level for any of the tester strains, with or without S9. Positive control agents performed as expected. Significant cytotoxicity was observed at 3276.8 ug/plate, based on depletion of background lawn.	
Test substance	: Obtained from Tokyo Kassei Kogyo Co. Ltd.	
Reliability	: (2) valid with restrictions Study conducted consistent with but prior to development of US GLPs effective 6/79; project was conducted in association with US EPA. Study results are confirmed in additional literature references (Simmon et al. 1977. Dev. Toxicol. Environ. Sci. 2:249-258 and Suzuki et al. 1983. Mut. Res. 120:105-110).	
Flag 06.12.2002	: Critical study for SIDS endpoint	(11)
Type	: Cytogenetic assay	
System of testing	: CHO (Chinese Hamster Ovary) cells in vitro assay	
Concentration	: 0, 50, 160, and 500 ug/ml	
Cycotoxic conc.	:	
Metabolic activation	: with and without	
Result	: negative	
Method	: other	
Year	: 1987	
GLP	: yes	
Test substance	:	
Method	: Test consisted of concurrent and positive (TEM) controls and at least 3 doses of test material. A single flask per dose was used. Cells were incubated in McCoy's 5A medium with test agent for 12 hrs (cells were treated with test agent and S9 for 2 hrs), colcemid added and cells incubated for an additional 2 hrs and harvested. 100 first-division metaphase cells were scored blind from prepared slides for each dose level. Classes of aberrations were recorded and included simple, complex and other abnormalities. Statistical analyses (linear regression analysis and, for absolute increases, methodology of Margolin et al 1983) was conducted on both the dose-response curve and individual dose points, significance was determined as p<0.05 for single data points and p<0.015 for trend.	
Result	: Did not induce Chrom Abs in CHO cells with or without metabolic activation at any test level.	
Reliability	: (2) valid with restrictions Combined Chromosomal Aberration and SCE study followed NTP study design. Was well documented and useful for regulatory purposes. SCE study portion was reported as equivocal as "the very slight increase in SCEs without S9 is unlikely to be meaningful despite the positive trend test; the other results were negative".	
Flag 02.12.2002	: Critical study for SIDS endpoint	(6)

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5. Toxicity

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Date 09.12.2002

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

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7. Risk Assessment

Id 121-73-3
Date 09.12.2002

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT

I U C L I D

Data Set

Existing Chemical	: ID: 88-73-3
CAS No.	: 88-73-3
EINECS Name	: 1-chloro-2-nitrobenzene
EINECS No.	: 201-854-9
TSCA Name	: Benzene, 1-chloro-2-nitro-
Molecular Formula	: C6H4ClNO2

Producer Related Part	
Company	: Solutia Inc.
Creation date	: 04.04.2002

Substance Related Part	
Company	: Solutia Inc.
Creation date	: 04.04.2002

Memo	:
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Printing date	: 09.12.2002
Revision date	:
Date of last Update	: 06.12.2002

Number of Pages	: 26
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Chapter (profile)	: Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile)	: Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	: Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1. General Information

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1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : = 32.5 °C
Sublimation :
Method : other
Year : 1996
GLP : no data
Test substance : other TS
Method : not reported
Test substance : o-Chloronitrobenzene
Reliability : (2) valid with restrictions
Obtained from accepted reference text and value cited as Peer reviewed in
HSDB (2002) for o-chloronitrobenzene and in EPA draft CHIP for oNCB
(1983)
Flag : Critical study for SIDS endpoint
02.12.2002 (19)

2.2 BOILING POINT

Value : = 245.7 °C at
Decomposition :
Method : other
Year : 1996
GLP : no data
Test substance : other TS
Method : not reported
Test substance : o-chloronitrobenzene
Reliability : (2) valid with restrictions
Obtained from accepted reference text and value cited as Peer reviewed in
HSDB (2002) for o-chloronitrobenzene and in EPA draft CHIP for oNCB
(1983)
Flag : Critical study for SIDS endpoint
02.12.2002 (19)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .0575 hPa at 20° C
Decomposition :
Method : other (measured)
Year : 1999
GLP : no data
Test substance : other TS
Method : not reported
Test substance : o-Chloronitrobenzene
Reliability : (2) valid with restrictions
Obtained from accepted reference text and similar value cited in EPA draft
CHIP for oNCB (1983)
Flag : Critical study for SIDS endpoint
12.11.2002 (1)

2.5 PARTITION COEFFICIENT

Log pow : = 2.24 at ° C
Method : other (measured)
Year : 1971
GLP : no data
Test substance : other TS
Method : not reported
Test substance : o-Chloronitrobenzene
Reliability : (2) valid with restrictions
Obtained from standard reference text and cited as Peer reviewed in HSDB (2002) for o-NCB and the EPA draft CHIP (1983) for o-NCB.
Flag : Critical study for SIDS endpoint
02.12.2002

(8)

2.6.1 WATER SOLUBILITY

Value : = 307.2 mg/l at 25 ° C
Qualitative : moderately soluble (100-1000 mg/L)
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1995
GLP : no data
Test substance : other TS
Method : calculated; group contribution method. Group contribution methods allow for the estimation of water solubility based on the chemical structure of a given compound. Values assigned to substructural units (referred to as "fragments") are summed to give a final solubility for the entire compound. The fragment values used in this method were compiled from the KWB1 (Klopman, G, S Wang and DM Balthasar. 1992. J. Chem. Inf. Comput Sci. 32:474-482) and WYMW (Wakita, K, M Yoshimoto, S Miyamoto and H Watanabe. 1986. Chem. Pharm Bull 34:4663-4681) group contribution methods. Additionally, as this method traditionally models liquids better than solids, a melting point term was included to improve the values generated for compounds considered solids.
Result : The estimated water solubility (Sw) of o-Chloronitrobenzene was reported as log Sw [mol/l] = -2.71. Based on a molecular weight of 157.56 g/mol, Sw = 307.2 mg/l.
Test substance : o-Chloronitrobenzene.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
06.12.2002

(7)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2. Physico-Chemical Data

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2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3. Environmental Fate and Pathways

Id 88-73-3

Date 09.12.2002

3.1.1 PHOTODEGRADATION

Type	: other
Light source	: Xenon lamp
Light spect.	: nm
Rel. intensity	: based on Intensity of Sunlight
Direct photolysis	
Half-life t _{1/2}	:
Degradation	: 66 % after 5 hour(s)
Quantum yield	:
Deg. Product	: yes
Method	: other (measured)
Year	: 1979
GLP	: no data
Test substance	: other TS
Method	: One milliliter of o-chloronitrobenzene in n-hexane was put in 1 liter reaction vessel (either pyrex or quartz), followed by substitution of n-hexane vapor with air or nitrogen free from nitrogen oxides. TS was deposited in the reaction vessel, which corresponds to 1000 microliter gas if vaporized, and was irradiated at 25 to 30 degrees C for 5 hours with the Xenon lamp (ozone-less type, Ushio Co.). Disappearance rate measured via HPLC of parent TS. By-product identification was by GC-MASS.
Result	: Rate of disappearance was influenced by the intensity of light passing through either of two reaction vessels used in this experiment, i.e. pyrex and quartz. The rate of disappearance of ONCB in air free of nitrogen oxides, when tested in pyrex and quartz vessels, respectively, was 4.3% and 66%. When ONCB was tested in nitrogen free of nitrogen oxides in pyrex and quartz vessels, respectively, disappearance rates were 9.5% and 93%. The reaction by-products in air free from nitrogen oxides were 2-chloro-6-nitrophenol and 2-chloro-4-nitrophenol. The reaction by-product in nitrogen free from nitrogen oxides was o-chlorophenol.
Test substance	: Laboratory synthesized, purity unspecified.
Reliability	: (2) valid with restrictions Published literature source which corroborates photodegradation potential of ONCB.
Flag	: Critical study for SIDS endpoint
06.12.2002	(5)
Type	: other
Light source	:
Light spect.	: nm
Rel. intensity	: based on Intensity of Sunlight
Direct photolysis	
Half-life t _{1/2}	: = 62.5 day
Degradation	: % after
Quantum yield	:
Deg. Product	:
Method	: other (calculated)
Year	: 2002
GLP	: no
Test substance	:
Method	: AOPWIN, v. 1.90; vapor phase of o-chloronitrobenzene is susceptible to reaction with photochemically-produced hydroxyl (OH) radicals.
Result	: The 2nd order rate constant for reaction with hydroxyl radicals was calculated as 0.1714E-12 cm ³ /(molecule*sec.). Based on 1.5E6 OH molecules/cm ³ and assuming 12 hours of sunlight per day, the estimated photo-oxidation half-life is 62.4 days (~1500 hrs).
Reliability	: (2) valid with restrictions Supplemental information as the previous study fulfills this HPV data

3. Environmental Fate and Pathways

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requirement. Estimated value based on model recommended by US EPA.

(4)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	other
Air (level I)	:	6.51
Water (level I)	:	33.5
Soil (level I)	:	59.8
Biota (level II / III)	:	
Soil (level II / III)	:	.162
Method	:	other
Year	:	2002
Method	:	Level III Fugacity Model employed using EPIWIN, v. 3.10. Physical properties for ortho-chloronitrobenzene have been cited in this report and include: water solubility = 307.2 mg/l; vapor pressure = 0.043 mm Hg (~ 0.0575 hPa); log Kow = 2.24 and melting point of 32 deg. C. Emissions rates were set at 1000 kg/hr for air (half life of 1500 hr), water (half life of 900 hr), soil (half life of 900 hr) and sediment (half life of 3600 hr). Persistence Time: 576 hrs. The second soil listing is the projected sediment loading.
Reliability	:	(2) valid with restrictions Estimated values based on model recommended by US EPA with ONCB specific entry data.
Flag	:	Critical study for SIDS endpoint

06.12.2002

(4)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic, non-adapted
Concentration	:	1mg/l related to Test substance 10mg/l related to Test substance
Contact time	:	10 month
Degradation	:	= 11 - 48 % after 24 hour(s)
Result	:	
Deg. Product	:	
Method	:	other
Year	:	1965
GLP	:	no

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Test substance	: other TS	
Method	: SCAS test conducted over a 10-month period per J. Am. Oil Chemists Society methods (JAOCS, 1965, 42:986 and JAOCS, 1965, 46:432). Feeding rate started at 1 mg/24-h and raised in 1 mg increments to 5 mg over 28 days and held at 5 mg/24-h for 4 months, then raised to 10 mg/24-h. Twenty mL samples of mixed liquor (activated sludge + liquor) were taken 1 hour after each addition and at the end of the aeration cycle via sidearm stopcock. The mixed liquor was extracted and analyzed via UV spectroscopy according to laboratory SOPs. Spike recovery experiments were 99.1 +/- 4.7%. Inoculum came from municipal sludge.	
Result	: Average disappearance rate, days 75- 120 (5 mg feed level, high aeration rate) was 10.6 +/- 9.4 % over a 24-h cycle; over the next 60 days (5 mg feed rate, high aeration rate) it was 37.5 +/- 8.8 % over a 24-h cycle, and over the last two weeks (10 mg feed level, low aeration) it averaged 47.7 +/-8.1% per 24-hr cycle.	
Test substance	: Commercial grade ONCB with purity of 98.9%.	
Reliability	: (2) valid with restrictions Well documented study which conformed to pre-OECD/EPA guidance for SCAS testing; methodology used subsequently codified into test guidance for # 302A.	
Flag 06.12.2002	: Critical study for SIDS endpoint	(16)
Type	: aerobic	
Inoculum	: other	
Concentration	: .0961mg/l related to Test substance related to	
Contact time	: 56 day	
Degradation	: 6 % after 56 day	
Result	:	
Deg. Product	:	
Method	: other	
Year	: 1971	
GLP	: no	
Test substance	: other TS	
Method	: River Die-Away test (RDA). River water was obtained from the Mississippi River near St. Louis, Mo. USA. Settled water (2 days) was added (250 ml) to 500 ml narrow-mouth bottles. Distilled water controls (with test substance) were prepared similarly to assess sorption to glass and volatilization. TS was added in 5 microliter volumes prepared with 5% (w/v) ethanol. Bottles were sealed with foil-lined caps and stored at room temperature in the dark. A positive control (LAS Reference # 2 -dodecene-1) was prepared similarly and used to verify the biological activity. Periodically, chemical analyses were made by sacrificing a bottle with TS and a control. A 25 mL aliquot of hexane was injected into the bottle, the bottle vigorously shaken, and the phases allowed to separate. A portion of the hexane was collected, transferred to a 2 mL cell and the UV absorption determined. Recoveries of spiked samples for the TS were 91.6%.	
Result	: Losses from the distilled water control were insignificant (0.996 mg/L at day 0 and 1.004 mg/L at day 56. TS concentration was 0.961 mg/L at day 0 and 0.904 mg/L at day 56 (loss of 5.93% due to biodegradation in 56 days).	
Test substance	: Commercial grade ONCB with purity of 99%.	
Reliability	: (2) valid with restrictions Supplemental information as previously reported study fulfills HPV endpoint.	
06.12.2002		(16)

3.6 BOD5, COD OR BOD5/COD RATIO

3. Environmental Fate and Pathways

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Date 09.12.2002

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: semistatic
Species	: <i>Poecilia reticulata</i> (Fish, fresh water)
Exposure period	: 14 day
Unit	: mg/l
Analytical monitoring	: yes
LC50	: = 30.03
Method	:
Year	: 1981
GLP	: no data
Test substance	: other TS
Method	: Methodology fully summarized in Koenemann, 1981. Toxicology 19:209-221. Guppies used in testing were raised in the laboratory of the Department of Veterinary Pharmacology, Pharmacy, and Toxicology, University of Utrecht, The Netherlands. Fish used in the 14-day toxicity tests were 2-3 months old at test initiation. Tests were conducted in 1.5 liter standard jars. Fish were acclimated for a minimum of 12 days prior to testing. The test water used was prepared standard water, corresponding to very soft tap water. Test water had a hardness of 25 mg/l (as CaCO ₃). Water quality parameters measured during the test (at least 4 days over the exposure period, before and after solution renewal) included oxygen content of >4.5 mg/L; temperature of 21-23 deg.C. and pH of 6.8-7.2. Test concentrations were analyzed (at least every 4 days over the exposure period, before and after solution renewal), by gas chromatography with both electron capture and flame-ionization detection (GC-ECD/FID). Ten fish each were exposed to a geometric progression of test substance concentrations. Mortality and abnormal signs of behavior were recorded over the exposure period. LC50 value was calculated from mortality data by logit transformation and were based on nominal concentrations.
Result	: The 14-d LC50 for ONCB was 2.28 umoles/l (based on a molecular weight of 157.6 g/mol, the LC50 can be expressed as 30.03 mg/l). Authors reported that measured concentrations of test solutions were at least 80% of nominal. Test organisms generally showed loss of balance, lethargy and increased appetite at low concentrations of the test substance. At high concentrations, cyanosis was noted in some test organisms.
Test substance	: Commercial grade o-chloronitrobenzene with purity of 99%.
Reliability	: (2) valid with restrictions Well documented study which lacks some individual information (i.e. lengths/weights of fish); actual concentrations not listed and no information on control group reported.
Flag	: Critical study for SIDS endpoint
06.12.2002	(3)
Type	: other
Species	: other
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no
LC50	: c = 69.5
Method	: other
Year	: 2002
GLP	: no
Test substance	: other TS
Method	: calculated using ECOSAR
Result	: An acute fish 96-hr LC50 was calculated using ECOSAR from US EPA; the SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR

4. Ecotoxicity

Id 88-73-3

Date 09.12.2002

Test substance : o-Chloronitrobenzene
Reliability : (2) valid with restrictions
Provided as Supplementary information; model used has been accepted by US EPA.
12.11.2002 (18)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
NOEC : = 12.5
EC50 : = 41
Method : other
Year : 1975
GLP : no
Test substance : other TS
Method : Followed EPA method # 660/3-75-009. Ten 24-h old D. magna were tested at 24 deg. C in a series of three replicates per test concentration. Test concentrations were 6.25, 12.5, 25, 50, 100 mg/L plus clean water and solvent (0.5 mg/L DMF) controls. Tests were conducted in well water from St. Peters, Mo. USA. Test concentrations were not measured. Daphnids were not fed. Tests were conducted in 250-mL beakers containing 200 mL of solution. Dissolved oxygen was monitored to ensure the concentration did not fall below 2 mg/L before the end of the test. Water quality was measured according to SOPs for dissolved oxygen, pH, alkalinity, hardness and temperature and no significant changes were observed in any parameter. The estimated EC50 and 95% confidence limits were determined using EPA statistical procedures.
Result : There were no control mortalities, plus no partial and total mortalities in the test vessels with test substance. The 24-h EC50 (95%CL) = 45 (25-100) mg/L; the 48-h EC50 (95%CL) = 41 (35.7-47.6) mg/L; The NOEC = 12.5 mg/L. Water temp. was 24 deg. C in all test vessels, pH ranged between 7.0 - 7.2, alkalinity measured between 146-296 mg/L, dissolved oxygen ranged between 7.6-10.7 and hardness was between 162-304 mg/L.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
06.12.2002 (15)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
EC50 : c = 95.7
Method : other
Year : 2002
GLP : no
Test substance : other TS
Method : An acute Daphnia 48-h LC50 was calculated using ECOSAR, from the US EPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.
Reliability : (2) valid with restrictions Provided as supplemental information in that an acceptable study meets this HPV endpoint.
Provided as supplemental information in that an acceptable study meets this HPV endpoint.
12.11.2002 (18)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
EC50	:	= 24
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Method	:	NEN 6501- "Determination of acute toxicity with Daphnia magna". Dutch Standardization Organization, Rijswijk, The Netherlands. The 48-h acute test was conducted with three CNB isomers, including o-nitrochlorobenzene. The LC50 and 95% confidence limits were determined by the Litchfield and Wilcoxon (1949) method.
Result	:	LC50=24 mg/L with CL of 18-32 mg/L. Relative toxicity of the three CNB isomers were (high to low): para>meta>ortho.
Test substance	:	o-nitrochlorobenzene with purity of 99%, obtained from Merck.
Reliability	:	(4) not assignable Provided as supplemental data in that this study, as published, provides insufficient individual data to allow higher categorization. Provided as supplemental data in that this study, as published, provides insufficient individual data to allow higher categorization.

06.12.2002

(9)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	biomass
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC10	:	m = 11
EC50	:	m = 34
Method	:	other
Year	:	1988
GLP	:	no data
Test substance	:	other TS
Method	:	DIN 38412, Part 9- The green alga S. subspicatus (Strain 8681 SAG) was used to conduct a modified cell multiplication inhibition test. A stock solution of the test substance was prepared in double-distilled water and diluted to prepare a series of test concentrations ranging from 0.80-100 mg/L. The test was conducted in capped 250 ml Erlenmeyer flasks. Eight (8) replicates of each concentration were tested. Flasks were inoculated with the cell suspension (cell concentration of 10E5 cells/ml in each flask), placed on a white surface, protected from sunlight, shaken daily, and exposed to constant artificial lighting. The temperature was maintained at 24 +/- 1 deg C. and the relative humidity was 50%. A control group (8 replicates) was tested concurrently. On each measurement day, 50 ml were collected from each of two flasks from each test concentration or the control. The extinction value of the monochromatic radiation (578 nm wavelength) of the cell suspension was determined for each test concentration and the control. Samples were collected and measurements were made at the beginning of the test and after 24 and 48 hrs. Biomass determination was based on measurement of optical density (turbidity). EC values were determined by regression analysis.
Result	:	Mean measured values of control group at 48 hrs were : extinction value- 0.068; Biomass-3.6x10E5 cells/ml. Results of the cell multiplication inhibition test of TS were: 48-hr Biomass EC10=11 mg/L; 48-h Biomass

	EC50= 34 mg/L. The 48-h average specific growth rate EC10= 19 mg/L.; the 48-h average specific growth rate EC50= 75 mg/L.	
Test substance	: o-chloronitrobenzene.	
Reliability	: (2) valid with restrictions Small deviations from standard study design, including less duration used, and limited information presented on each test concentration at each measurement point.	
Flag 02.12.2002	: Critical study for SIDS endpoint	(6)
Species	: other algae	
Endpoint	:	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
Analytical monitoring	:	
EC50	: c = 48	
Method	: other	
Year	: 2002	
GLP	: no	
Test substance	: other TS	
Method	: Method of calculation of an acute green algal 96-h LC50 used ECOSAR from USEPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.	
Reliability	: (2) valid with restrictions Provided as Supplemental information as a previous study fulfills this HPV endpoint.	
02.12.2002		(18)
Species	: Chlorella pyrenoidosa (Algae)	
Endpoint	: other	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
Analytical monitoring	: no data	
EC50	: m = 6.9	
Method	: OECD Guide-line 201 "Algae, Growth Inhibition Test"	
Year	: 1984	
GLP	: no data	
Test substance	: other TS	
Method	: The 96-h EC50 for effects on yield and 95% confidence limits were determined by the method of Kooyman et al, 1983 and followed guidance of OECD # 201.	
Result	: The 96-h EC50 and confidence limits were 6.9 (5.7-8.4) mg/L.	
Test substance	: o-Chloronitrobenzene obtained from Merck with purity of 99%.	
Reliability	: (4) not assignable Provided as Supplemental data, in that this study, as published, provides insufficient individual data to allow higher categorization.	
06.12.2002		(9)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4. Ecotoxicity

Id 88-73-3
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4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: rat
Strain	: Sprague-Dawley
Sex	: male/female
Number of animals	: 20
Vehicle	: other
Value	: 560 mg/kg bw
Method	: other
Year	: 1973
GLP	: no
Test substance	: other TS
Method	: Administered by single oral gavage in corn oil as vehicle to groups of male and female (total of 5 mixed sex per group) rats given 398, 501, 631 and 764 mg/kg ONCB. Clinical signs of toxicity and deaths were recorded daily for the 7-day observation period. Body weights were recorded on test days 0 and 7. Necropsies were performed after death and on all rats surviving to day 7. Food and water were provided ad libitum and temp., humidity and light were controlled. LD50 value and CI were calculated by method of deBeer, J. Pharmacol Experiment. Ther. 86:1.
Result	: OLD50 = 560 mg/kg with CI of 535-585 mg/kg. Deaths observed were: 1/5 @ 398 mg/kg, 2/5 @ 501 mg/kg, 4/5 @ 631 mg/kg, and 5/5 @ 764 mg/kg. Deaths occurred during days 1-4 of testing with the majority occurring within the first two days of the test. Toxicologic signs observed were increased weakness and ocular discharge. Decedents exhibited hemohaggic lungs and discolored livers, spleens, and kidneys at necropsy. After 7 days, survivors exhibited lung congestion and darkened spleens and kidneys at necropsy.
Test substance	: Used commercial grade, > 99% pure, dosed in 10% corn oil and heated to 115 deg F before gavaging.
Reliability	: (2) valid with restrictions Conducted with fewer animals than OECD guideline 401 and prior to inception of US EPA GLPS. The shorter duration for observation than found in the OECD test guidance for this study type did not affect its outcome or the conclusions drawn, as all deaths occurred within the first two days of the study with surviving animals recovering within the latter portion of this study. Test results (OLD50 values ranging between 144-560 mg/kg) are consistent with additional studies for this endpoint in the ECB IUCLID (2002) for ONCB
Flag	: Critical study for SIDS endpoint

02.12.2002

(17)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5. Toxicity

Id 88-73-3

Date 09.12.2002

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	: rat
Sex	: male/female
Strain	: Fischer 344
Route of admin.	: inhalation
Exposure period	: 6 hr/day
Frequency of treatment	: 5 days per week for 13 weeks
Post obs. period	: none
Doses	: 0, 1.1, 2.3, 4.5, 9 or 18 ppm
Control group	: yes
NOAEL	: < 1.1 ppm
Method	: OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	: 1989
GLP	: yes
Test substance	: other TS
Method	: Groups of 10 male and 10 female F-344 rats were exposed in whole body stainless steel and glass chambers to vapors containing 0, 1.1, 2.3, 4.5, 9 or 18 ppm ONCB for 6 hr/day, 5 days per week, for 13 weeks. Vapor was generated by heating ONCB first in a water bath, then in a hot-oil bath and passing metered nitrogen over the test material prior to introduction into the test chamber. Levels of flow were registered using automated data acquisition and control systems. Air concentrations were measured using GC/EC. Due to the low volatility of ONCB, it was concluded that the level achieved in a vapor state was essentially the maximum technically achievable. Animals were individually caged, food and water administered ad libitum, and a 12 hr light/dark cycle employed. All animals were assessed for morbidity and mortality daily, and weekly examined for clinical toxicity and recording of body weights. At termination of the study (13 weeks) all animals were necropsied and a full set of over 40 tissues and organs were examined microscopically for all high dose and control animals; target organs were examined for animals from lower dose groups. Organ weights and relative weights were assessed for all animals after 13 weeks of testing and included the following organs: heart, kidney, lung, liver, spleen, testis and thymus. The following hematology parameters were assessed on study day 1 (Methemoglobin only), 4, 23 and at 13 weeks from all rats from each study group: HCT, HGB, RBC, RETIC, MCV, MCH, MCHC, PLAT, WBC, MET, and WBC differentials. Similarly, the following clinical chemistry parameters were measured from all rats at similar time points as hematology: BUN, CREAT, TPROT, ALB, GLOB, ALT, AP, CK, SDH and bile acids. Williams parametric multiple comparison procedure was employed to statistically assess group-wise comparison of organ and body weights. Shirley's test for nonparametric analysis was used for clinical chemistry and hematology assessments. P<0.05 and 0.01 were used in all cases.
Remark	: In a satellite group used to assess reproductive parameters, no significant changes were seen in groups of females, but lower epididymal wts, spermatid heads /testis and spermatid count in the 18 ppm male dose group was noted.
Result	: Following are treatment-related effects noted at each dose group: 1.1 ppm - Males - increased MET, SDH, and RE (Respiratory Epithelium) hyperplasia; females - increased. MET and RE hyperplasia. 2.3 ppm - Males - increased MET, SDH, ALB, ALT, bile acids, liver wts (a/r), RE

	<p>Males - increased MET,SDH, ALB, ALT, bile acids, liver wts (a/r), RE hyperplasia and decreased HCT; females - increased MET, Seg neutro, RE hyperplasia. 4.5 ppm - Males - decreased HCT, HGB, RBC, and increased MET, SDH, ALB, ALT, AP, BA, liver wt (a/r), RE hyperplasia and kidney cytoplasmic pigmentation; females - decreased HCT, HGB, RBC, and inc. MET, Seg neut, ALB, AP, liver wt (a/r) and spleen wt (a/r) and RE hyperplasia. 9 ppm - Males - decreased HCT, HGB, RBC, Plat, and increased in RETIC, Nucl. RBC, MET, SDH, ALB, ALT, AP and BA, kidney wt (r) and liver wt (a/r), liver basophilia, kidney pigmentation and RE hyperplasia; females - decreased HCT, HGB, RBC, MCH, MCHC, PLAT, and increased RETIC, MET, SDH, SLB, AP, liver wt (a/r), spleen wt (a/r), and liver basophilia, kidney pigmentation, and RE hyperplasia. 18 ppm - Males - decreased HCT, HGB, RBC, PLAT, and increased RETIC, Nucl RBC, MET, SDH, ALB, ALT,AP, BA, kidney wt (r), liver wt (a/r), splenic wt (a/r), liver basophilia, kidney pigmentation, splenic congestion and RE hyperplasia; Females - decreased HCT, HGB, RBC, MCV, MCH, MCHC, PLAT and increased RETICS, MET, Nuc. RBC, SDH, ALB, ALT, AP, kidney wt (a/r), liver wt (a/r), splenic wt (a/r), liver basophilia, kidney pigmentation, splenic congestion, and RE hyperplasia.</p> <p>No deaths were observed in this study nor were there treatment-related effects seen in body weight gain. No clear clinical signs of toxicity were observed. Hematology findings were found consistently in ONCB-treated groups and was consistent with methemoglobinemia and normocytic, normachromic anemia by the end of the study. Target organs identified in this study included the liver, spleen, kidney and nasal cavity (dorsal meatus and most anterior turbinate). Based on microscopic findings in the respiratory epithelium and methemoglobinemia seen at 1.1 ppm, a NOEL was not established in this study.</p>
Test substance	: Commerical grade ONCB analyzed confirmed purity > 99%.
Reliability	: (1) valid without restriction
Flag	: Critical study for SIDS endpoint
02.12.2002	(10)
Species	: rat
Sex	: male/female
Strain	: Sprague-Dawley
Route of admin.	: inhalation
Exposure period	: 6 hr/day
Frequency of treatment	: 5 days per week for 4 weeks
Post obs. period	: none
Doses	: 0, 10, 30, or 60 mg/m3
Control group	: yes
NOAEL	: = 10 mg/m3
Method	: OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year	: 1982
GLP	: yes
Test substance	: other TS
Method	<p>: Groups of 15 male and 15 female SD rats were exposed via whole body in stainless steel and glass inhalation chambers to airborne concentrations of 0, 10, 30 or 60 mg/m3 ONCB for 6 hr/d, 5 days/wk for 4 weeks. Concentrations of ONCB were determined at least 3X daily using UV spectrophotometry. Parameters monitored in this study included daily morbidity and mortality checks, weekly detailed clinical observations and body weights. Hematology parameters (HGB, RBC, HCT, RETIC, MET, clotting time, RBC morph. and total and differential leukocytes) and clinical chemistries (BUN, SGPT,AP, GLU, ALB, TPROT, GLOB, K, CL, CA, PHOS) were analyzed at days 0 and just prior to termination (MET also analyzed after 2 weeks of testing) for 10 rats/sex/group. Ophthalmoscopic exams were conducted on all rats prior to study start and at termination. Organ (brain, testes, heart, kidneys, liver, lungs, spleen) weights and weight ratios were recorded at terminal sacrifice for all rats on test. Microscopic</p>

	ratios were recorded at terminal sacrifice for all rats on test. Microscopic examination of over 40 tissues and organs was performed on 10 rats/sex from the high dose and controls and spleens from 10 male and 10 female mid and low dose animals. Gormori's stain was used to semiquantitate the degree of hemosiderosis. A Bartlett's test was performed on study data to determine the degree of equality of variance. Parametric procedures (Snedecor and Cochran followed by Dunnett's test) were used for parametric parameters. The Kruskal-Wallis test, followed by Dunn's Summed Rank test, were used for nonparametric parameter analysis. $P < 0.05$ was used in all cases.
Result	: Cumulative chamber concentrations were 0, 9.9, 30 and 59 mg/m ³ ; thus good correlation occurred between nominal and analytical values. No effects were seen in ocular toxicity, body weight gain, or clinical signs and no deaths occurred. Effects of treatment were limited to increases in methemoglobin (MET), anemia, organ weight changes (liver, kidney and spleen) and microscopic findings (extramedullary hematopoiesis and hemosiderosis) seen in the spleen. Following are the significant effects seen at each dose level - 10 mg/m ³ : Males - liver wt increase (rel. wt only), small non-stat. significant increase in MET; Females - nonstatistically significant increase MET. 30 mg/m ³ - Males - increased MET, liver wt (a/r), Kidney wt (a/r), spleen wt (a/r), small increase in splenic path.; Females - decreased RBC, HGB, HCT, and increased MET, liver wt (a/r), kidney wt (a/r) and splenic wt (a/r) plus slight spleen microscopy; 60 mg/m ³ - Males - decreased RBC, HGB and increased MET, RET, liver, kidney and spleen wts (all a/r) and pathology of the spleen; Females - decreased RBC, HGB, HCT and increased HCT, MET, RET, and liver, kidney and spleen wts (a/r) and pathology of the spleen.
Test substance	: Commercial grade ONCB with purity > 99%.
Reliability	: (1) valid without restriction Well documented study, conducted according to GLPs and meeting OECD guidance # 412; Supplemental information for HPV as a study of longer duration has been used to fulfill this endpoint.
06.12.2002	(13)
Species	: rat
Sex	: no data
Strain	: other
Route of admin.	: oral unspecified
Exposure period	: up to 7 months
Frequency of treatment	: daily
Post obs. period	:
Doses	: 70 mg/kg/d for 20 days; 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months
Control group	: yes
NOAEL	: = .025 mg/kg bw
Method	: other
Year	: 1967
GLP	: no
Test substance	: other TS
Method	: Peroral treatment of 20 albino rats at 70 mg/kg for 20 days, followed by peroral administration of ONCB to groups of rats at 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months. Measured indices reportedly included hematology, liver function (blood and urine) and peripheral blood pathology.
Result	: 0/20 rats treated with 70 mg/kg ONCB for 20 days died. Groups of rats treated for 7 months exhibited marked changes in peripheral blood. Methemoglobin levels were increased only during the seventh month of testing in the HD group; elevations occurred only at 5 mg/kg ONCB. Hemoglobin was reduced and reticulocytes, serum alkaline phosphate and urinary bilirubin were elevated along with presence of Heinz bodies in erythrocytes at 5 mg/kg/d. The NOEL was 0.025 mg/kg/d.
Conclusion	: Comparative study using ONCB, MN CB and PNCB. Concluded that PNCB was the most toxic isomer following systemic exposure, MNCB was

was the most toxic isomer following systemic exposure, MNCB was intermediate, and ONCB was the least systemically toxic of the three isomers tested. All isomers exhibited essentially the same pattern of toxicity.

Reliability : (4) not assignable
Supplemental information, as this report provides but a summary of results without sufficient detail to be classified higher.

06.12.2002

(2)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Salmonella typhimurium strains TA100, TA98, TA1535 and TA1537
Concentration : 0, 10, 33, 100, 333, 1000 ug/plate
Cycotoxic conc. : 1000 ug/plate
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"

Year : 1983
GLP : yes
Test substance : other TS
Method : Methodology used by NTP was based on Ames test plate incorporation assay and consistent with OECD 471. All tests were run in duplicate and three plates were assayed at each dosage for each run both with and without metabolic activation. S9 obtained from male S-D rats injected with Arochlor 1254 (500 mg/ml) five days before they were killed; all tester strains obtained originally from B. Ames; the high dose was designed to produce toxicity (reduced background lawn or solubility limits). Sterile DMSO was used as the solvent; negative (solvent) and positive controls (2-aminoanthracene, 4-nitro-o-phenylenediamine, sodium azide and 9-aminoacridine) were used as appropriate to detect mutagenicity with or without metabolic activation in each of the 4 tester strains used. A positive response was detected if a reproducible dose-related increase (>2X) was seen in revertant colonies according to a model described by Margolin et al, 1981).

Result : Positive in strain TA100 only with metabolic activation; inactive in TA100 without activation and in other tester strains with or without rat S9.

Test substance : purity greater than 99%
Reliability : (1) valid without restriction
Consistent with OECD guideline 471 and conducted according to GLPs.

Flag : Critical study for SIDS endpoint

06.12.2002

(12)

Type : Cytogenetic assay
System of testing : Chinese Hamster Ovary Cell in vitro assay
Concentration : 50 - 500 ug/mL
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1987
GLP : yes
Test substance : other TS
Method : Study conducted according to NTP study design; testing involved 2 labs and included 2 tests (1 per lab) without S9 and three tests (repeat at one lab) with S9. The latter used SD male rat Arochlor 1254-induced liver homogenate. Cell cultures were handled to prevent photolysis of Brdu-substituted DNA. Each test consisted of concurrent solvent and positive controls and at least 3 dose levels. Cells were incubated in McCoy's 5A

	medium with test agent for 14 hours (ONCB was found to induce cell cycle delay, thus 18.5 hrs was used in one test), colcemid added and incubated for an additional 2 hrs and harvested and processed. 100 first-division metaphase cells (200 cells per dose group were used in follow up studies to address equivocal results) were scored blind from prepared slides for each dose level. Classes of aberrations were recorded and included simple, complex, and other abnormalities. Statistical analyses (Armitage trend test; Margolin multiple comparison test) were conducted on both the dose-response curve and individual dose points; significance was determined as $p < 0.05$ for single data points and $p < 0.015$ for trend.
Result	: Both tests using ONCB without metabolic activation resulted in equivocal and then negative results; no. of aberrant cells in the solvent control (DMSO), and at 16, 50 and 160 ug/ml (100 metaphases used) were 2, 8, 8, and 11; confirmatory test used 0, 47, 101 and 216 ug/ml which resulted in no. of aberrant cells of 3, 2, 0, 2 (used 200 metaphase cells). The initial test with S9 resulted in a negative finding, as the no. of aberrant cells were 4 (DMSO control), 6 (50 ug/ml), 6 (160 ug/ml) and 6 (500 ug/ml); Subsequent studies using top doses of 465 and 500 ug/ml yielded 22 and 23 aberrant cells, respectively, vs a control value of 3 and thus was considered weakly positive.
Conclusion	: ONCB is considered to be a weakly positive clastogen in the CHO in vitro assay only with metabolic activation.
Reliability	: (2) valid with restrictions Well documented, GLP study.
Flag	: Critical study for SIDS endpoint
06.12.2002	(11)

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	: other
Species	: mouse
Sex	: male/female
Strain	: CD-1
Route of admin.	: gavage
Exposure period	: 22 weeks
Frequency of treatment	: daily for study duration
Premating exposure period	
Male	: 7 days
Female	: 7 days
Duration of test	: 7 days pretest, 98 days breeding and up to 5 weeks for littering, and then until last litter is weaned
Doses	: 0, 40, 80, or 160 mg/kg/day
Control group	: yes
NOAEL Parental	: = 160 mg/kg bw
NOAEL F1 Offspr.	: = 160 mg/kg bw
Method	: other
Year	: 1992
GLP	: yes
Test substance	: other TS
Method	: Standard Continuous breeding protocol designed by NTP and published as Lamb, 1985. J. Amer. Coll. Toxicol. 4:163-171. Based on 2 week toxicity test to establish dose levels, animals are individually housed for 7 days,

	test to establish dose levels, animals are individually housed for 7 days, then cohoused in breeding pairs for 98 days, and allowed to propagate. During this period the following indices are recorded: clinical signs of toxicity, mortality, parental body weight and average consumption of water during representative weeks, fertility (e.g. no. of pairs producing a litter/number of breeding pairs), the no. of litters per pair, the no. live pups/litter, % pups born alive, sex ratio of pups and pup body weights after birth. The last litter born during the holding period (5 weeks) following the breeding period was reared until weaning. Thereafter treatment of the F1 animals was initiated and these animals used for assessment of second generation fertility. For this phase, siblings were cohoused until sexual maturity, when 20 non-sibling males and females per treatment group were cohabitated for 7 days and then housed singly through delivery. Endpoints for this mating trial were the same as for the F0 generation. At termination of F0 and F1 generations, animals were necropsied and evaluations made for organ weights (livers, ovaries or testes and epididymides from 5 per group, control and HD), body weights, epididymal sperm motility, sperm morphology, sperm count and estrual cyclicity. Methemoglobin measurements and spleen weights were recorded for both the F0 and F1 generations. Proportional data were assessed statistically using the Armitage trend test, with each dose group compared to control using a chi-square analysis. Absolute body and organ weights were compared using Shirley's or Dunns test while dose related trends were identified by Jonckheere's test. Vaginal cytology was analyzed using an analysis of variance described by Morrison to test for simultaneous equality. A p value of <0.05 or <0.01 was used.
Result	: In the final litter of the holding period following the continuous breeding phase, pup weight gain during suckling was lower in all 3 treated groups vs. control; at weaning pups in the 160 mg/kg group weighed 12% less than controls. All other fertility and reproductive parameters were unaffected. F1 animals had significantly lower body weights at weaning but were significantly heavier than controls at mating and termination and thus not considered toxicologically significant. Thus, no adverse effects in reproductive endpoints were observed for F1 generation animals. Nonreproductive toxicity was observed similarly in both F0 and F1 animals from the 160 and 80 mg/kg dose groups and included: increased spleen and liver weights and methemoglobinemia.
Test substance	: Test material with analytically confirmed purity > 99%.
Conclusion	: Report concluded that "ONCB does not appear to be a reproductive toxicant, even in the presence of systemic toxicity, in Swiss CD-1 mice"
Reliability	: (2) valid with restrictions Well documented study using a unique protocol designed to provide reproductive toxicity evaluations.
Flag	: Critical study for SIDS endpoint
06.12.2002	

(10)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	: rat
Sex	: female
Strain	: Sprague-Dawley
Route of admin.	: gavage
Exposure period	: Gestation days 6 - 15
Frequency of treatment	: Once daily during the exposure period
Duration of test	: Study terminated on gestation day 21
Doses	: 0, 25, 75, 100 or 150 mg/kg/d
Control group	: yes
NOAEL Maternal.	: >= 25 mg/kg bw
NOAEL Teratogen	: >= 100 mg/kg bw

NOAEL Embryotoxicity	: ≥ 100 mg/kg bw
NOAEL Fetotoxicity	: ≥ 100 - mg/kg bw
Method	: OECD Guide-line 414 "Teratogenicity"
Year	: 1987
GLP	: yes
Test substance	: other TS
Method	: Groups of 25 mated female SD rats were originally dosed with 25, 75 or 150 mg/kg ONCB on gestation days 6-15; a control group of 25 mated female rats exposed only to corn oil served as a concurrent control. Due to significant mortality seen in the 150 mg/kg test group, an additional study group was added and treated with 100 mg/kg ONCB. Body weights, detailed physical examinations and individual food consumption were recorded on gestation days 0, 6, 10, 13, 16, and 21. Complete necropsies and examinations of the uterine contents were performed on all females in the 100 mg/kg group and below at time of sacrifice. Full-term fetuses were examined externally, sexed, weighed and prepared for teratogenic evaluation. Approximately one-half of the fetuses in each litter were processed for either visceral soft-tissue evaluations using Wilson's techniques or were used for skeletal evaluations. For interval data (body wts, wt changes, reproductive data) Bartlett's test was used to determine equality of variance and ANOVA and Dunnett's test used for parametric data while the Kruskal-Wallis test and Summed Rank test were used for nonparametric data. For incidence data (i.e. mortality rates, % and incidence of variations and malformations) comparisons were made using the Chi-square contingency table and the 2X2 Fisher Exact test using the Bonferroni inequality estimate; linear trend was evaluated using the Armitage test. Comparisons were made using the litter as the comparative entity. Both p values of <0.05 and 0.01 were reported..
Result	: Six rats died between gestation days 6-13 at 150 mg/kg; one animal each died at 75 and 100 mg/kg while no deaths occurred in the control or 25 mg/kg test group. Maternal weight gain in the 25 and 75 mg/kg groups was greater than that of the concurrent controls throughout the study. Females in the 100 mg/kg test group had a reduced weight gain throughout the treatment period. No significant clinical observations associated with toxicity were seen. Food consumption was similar in controls and 25 mg/kg animals; significant decreases in food consumption were observed at 75 and 100 mg/kg during gest. days 6-16. Early resorptions were significantly increased at 75 mg/kg, although a similar response was not observed in the 100 mg/kg dose group. Other reproductive parameters and fetal body weights in the ONCB treated groups were similar to their respective controls. No increase in external, soft tissue or skeletal malformations was observed up to 100 mg/kg. Animals from the 150 mg/kg group were omitted from reproductive assessment due to the large no. of deaths in this group. While an increase in cervical # 7 rib was noted in litters from the 25 and 75 mg/kg groups no such effect was observed in litters from dams treated with 100 mg/kg and thus was not considered attributable to treatment.
Test substance	: Test article $> 99\%$ pure and mixed in corn oil for administration in daily volumes of 10 ml/kg.
Reliability	: (1) valid without restriction Well conducted study meeting test and GLP guidance; Supplemental information as a Reproductive study has been used to fulfill this endpoint.

02.12.2002

(14)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

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6. References

Id 88-73-3
Date 09.12.2002

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7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT

I U C L I D

Data Set

Existing Chemical	: ID: 100-00-5
CAS No.	: 100-00-5
EINECS Name	: 1-chloro-4-nitrobenzene
EINECS No.	: 202-809-6
TSCA Name	: Benzene, 1-chloro-4-nitro-
Molecular Formula	: C6H4ClNO2

Producer Related Part	
Company	: Solutia Inc.
Creation date	: 04.04.2002

Substance Related Part	
Company	: Solutia Inc.
Creation date	: 04.04.2002

Memo	:
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Printing date	: 09.12.2002
Revision date	:
Date of last Update	: 06.12.2002

Number of Pages	: 29
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Chapter (profile)	: Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile)	: Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	: Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1. General Information

Id 100-00-5
Date 09.12.2002

1.0.1 OECD AND COMPANY INFORMATION

25.11.2002

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1. General Information

Id 100-00-5
Date 09.12.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : = 83.4 - °C
Sublimation :
Method : other
Year : 1991
GLP : no data
Test substance : other TS
Method : not referenced
Test substance : p-Nitrochlorobenzene
Reliability : (2) valid with restrictions
Citation from a reputable, universally accepted reference guide; value cited in the PNCB HSDB (2002).
Flag : Critical study for SIDS endpoint
25.11.2002 (7)

2.2 BOILING POINT

Value : = 242 - °C at 1013.25 hPa
Decomposition :
Method : other
Year : 1991
GLP : no data
Test substance : other TS
Method : not reported
Remark : Listed as 242 deg. C @ 760 mm Hg.
Test substance : p-Nitrochlorobenzene
Reliability : (2) valid with restrictions
Citation from a reputable, universally accepted reference guide; value cited in the PNCB HSDB (2002).
Flag : Critical study for SIDS endpoint
25.11.2002 (7)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .1253 - hPa at 20° C
Decomposition :
Method : other (measured)
Year : 1973
GLP : no
Test substance : other TS
Remark : Reported as 0.094 mm Hg @ 20 deg. C.
Test substance : p-Nitrochlorobenzene
Reliability : (2) valid with restrictions
Cited as peer-reviewed in PNCB HSDB (2002).
Flag : Critical study for SIDS endpoint
25.11.2002 (1)

2.5 PARTITION COEFFICIENT

Log pow	:	= 2.39 - at ° C	
Method	:	other (measured)	
Year	:	1989	
GLP	:	no data	
Test substance	:	other TS	
Method	:	Followed EPA methodology as defined in USEPA-600/4-79-032; Shake flask method using 6 replicates.	
Test substance	:	p-Nitrochlorobenzene	
Reliability	:	(2) valid with restrictions Value derived from well accepted study design and consistent with other measured values reported in the literature (i.e. Hansch and Leo, 1995, SRC. Howard, 1990. Handbook of Environmental Fate and Exposure for Organic Chemicals. Lewis Pub.)	
Flag	:	Critical study for SIDS endpoint	
04.12.2002			(8)

2.6.1 WATER SOLUBILITY

Value	:	= 154 - mg/l at 25 ° C	
Qualitative	:		
Pka	:	at 25 ° C	
PH	:	- at and ° C	
Method	:	other	
Year	:	1995	
GLP	:	no	
Test substance	:	other TS	
Method	:	Group contribution method for calculation allows for the estimation of water solubility based on the chemical structure of a given compound. Values assigned to substructural units (referred to as "fragments") are summed to give a final solubility for the entire compound. The fragment values used in this method were compiled from the KWB1 (Klopman, G, S Wang, and DM Balthasar. 1992. J. Chem. Inf. Comput. Sci. 32:474-482) and WYMW (Wakita, K, M Yoshimoto, S Miyamoto and H Watanabe. 1986. Chem. Pharm. Bull. 34:4663-4681) group contribution methods. Additionally, as this method traditionally models liquids better than solids, a melting point term was included to improve the values generated for compounds considered solids (i.e. melting point > 25 deg. C).	
Result	:	The estimated water solubility (Sw) of PNCB was reported as log Sw [mol/l] = 3.01. Based on a molecular weight of 157.56 g/mol, the Sw=154 mg/L.	
Test substance	:	p-Nitrochlorobenzene	
Reliability	:	(2) valid with restrictions Experimental value of 189.4 mg/l @ 25 deg C also reported in same reference; additional literature references cite values between 225-230 mg/l at 20 deg C (HSDB, 2002).	
Flag	:	Critical study for SIDS endpoint	
04.12.2002			(6)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2. Physico-Chemical Data

Id 100-00-5
Date 09.12.2002

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3. Environmental Fate and Pathways

Id 100-00-5
Date 09.12.2002

3.1.1 PHOTODEGRADATION

Type : other
Light source : Xenon lamp
Light spect. : - nm
Rel. intensity : - based on Intensity of Sunlight
Indirect photolysis
Sensitizer :
Conc. of sens. :
Rate constant : $\text{cm}^3/(\text{molecule} \cdot \text{sec})$
Degradation : - 98 % after 5 hour(s)
Deg. Product : yes
Method : other (measured)
Year : 1979
GLP : no data
Test substance : other TS
Method : Photochemical reactivity assay where 1 mL of PNCB in n-hexane was put in 1 L reaction vessel, followed by substitution of n-hexane vapor with air or nitrogen free from nitrogen oxides. PNCB was deposited in the reaction vessel, which corresponded to 1000 μL gas if vaporized and was irradiated at 25-30 deg. C for 5 hr with the Xenon lamp (ozone-less type, Ushio co.). Disappearance of TS measured by HPLC. Reaction by-products measured by GC-MASS.

Result : Rate of disappearance was influenced by the intensity of light passing through either of two reaction vessels used in this experiment, i.e. pyrex and quartz. The rate of disappearance of PNCB in air free of nitrogen, when tested in pyrex and quartz vessels, respectively, was 4.1% and 96%. When PNCB was tested in nitrogen free of nitrogen oxides in pyrex and quartz vessels, respectively, disappearance rates were 7.1% and 98%. The single reaction by-product identified in air free from nitrogen oxides was 4-Chloro-2-nitrophenol while p-chlorophenol was the only by-product identified in nitrogen free from nitrogen oxides.

Test substance : Laboratory synthesized, purity no reported.
Reliability : (2) valid with restrictions
This study supports the photodegradative capacity of PNCB.
Flag : Critical study for SIDS endpoint

06.12.2002

(4)

Type : other
Light source :
Light spect. : - nm
Rel. intensity : - based on Intensity of Sunlight
Indirect photolysis
Sensitizer : OH
Conc. of sens. : $1500000 \text{ molecule}/\text{cm}^3$
Rate constant : $.0000000000001714 \text{ cm}^3/(\text{molecule} \cdot \text{sec})$
Degradation : 50 - % after 62.4 day
Deg. Product :
Method : other (calculated)
Year : 2002
GLP : no
Test substance : other TS
Method : Used AOPWIN, v. 1.90 from EPIWIN, Syracuse Research Corp.
Result : Vapor phase of PNCB is susceptible to reaction with photochemically-produced hydroxyl (OH) radicals. The 2nd order rate constant for reaction with hydroxyl radicals was calculated as $0.1714\text{E}-12 \text{ cm}^3/(\text{molecule} \cdot \text{sec})$. Based on $1.5\text{E}6 \text{ OH molecules}/\text{cm}^3$ and assuming 12 hours of sunlight per day, the estimated photo-oxidation half-life is 62.4 days (~1500 hrs).
Test substance : p-Nitrochlorobenzene

3. Environmental Fate and Pathways

Id 100-00-5
Date 09.12.2002

Reliability : (2) valid with restrictions
Value obtained from EPA recommended estimation model.
06.12.2002 (3)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other
Air (level I) : 9.52
Water (level I) : 28.5
Soil (level I) : 61.8
Biota (level II / III) :
Soil (level II / III) : .171
Method : other
Year : 2002
Method : Estimation using measured values from this dossier were incorporated into EPIWIN from Syracuse Research Corp., a methodology based on Meylan, 1993 as adopted by MacKay et al. 1996. Second Soil entry included estimation in Sediments. Values employed were : Mo. Wt = 157.56, vapor pressure of 0.094 mm Hg. Log Kow of 2.39, a melting point of 83 deg. C, and water solubility of 154 mg/L. Half lifes for air, water, soil and sediment were included as 1500 hr, 900 hr, 900 hr, and 3600 hr, respectively; emissions loading was 1000 kg/hr for each medium.
Remark : Persistence Time was 506 hr.
Test substance : p-Nitrochlorobenzene
Reliability : (2) valid with restrictions
Estimated values based on model recommended by US EPA.
Flag : Critical study for SIDS endpoint
04.12.2002 (3)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : domestic sewage
Concentration : 1mg/l related to Test substance
10mg/l related to Test substance
Contact time :
Degradation : 34 - 66 % after 24 hour(s)
Result :
Deg. Product :
Method : other

3. Environmental Fate and Pathways

Id 100-00-5

Date 09.12.2002

Year	:	1973	
GLP	:	no	
Test substance	:	other TS	
Method	:	Semi-Continuous Activated Sludge (SCAS) test conducted over 10-month period, in accordance with J Am Oil Chemists Society methods (JAOCS, 1965, 42:986 and JAOCS, 1965, 46:432). Inoculum was municipal waste treatment sludge. Feeding rate started at 1 mg/24-h and was raised in 1 mg increments to 5 mg over 28 days, and held at 5 mg/24-h for 4 months, then raised again to 10 mg/24-h. Twenty mL samples of mixed liquor (activated sludge + liquor) were taken 1 hr after each addition and at the end of the aeration cycle, via sidearm stopcock. The mixed liquor was extracted and analyzed via UV spectroscopy. Spike recovery experiments were 95.9 +/- 1.5%.	
Result	:	Average disappearance rate, days 75-120 (5 mg feed level, high aeration rate) was 33.9 +/- 2.9% over a 24-h cycle; over the next 60 days (same parameters) the disappearance rate was 30.7 +/- 9.4% over a 24-h cycle; over the last two weeks (10 mg feed level, low aeration), disappearance rate averaged 65.7 +/- 14.4% per 24-h cycle.	
Test substance	:	PNCB presumably as commercial grade with purity > 99%.	
Reliability	:	(2) valid with restrictions Study conducted prior to codification of GLPs but considered well documented. Methodology used has subsequently been incorporated into a standardized international test guideline for this study type.	
Flag	:	Critical study for SIDS endpoint	
06.12.2002			(11)
Type	:	aerobic	
Inoculum	:	other	
Contact time	:	56 day	
Degradation	:	13.4 - % after 56 day	
Result	:		
Deg. Product	:		
Method	:	other	
Year	:	1973	
GLP	:	no	
Test substance	:	other TS	
Method	:	River Die-Away Test (RDA). River water was obtained from the Mississippi River near St. Louis, MO, USA. Settled water (2 days) was added (250 mL) to 500 mL narrow-mouthed bottles. Distilled water controls (with test substance) were prepared similarly to assess sorption to glass and volatilization. PNCB was added in 5 uL volumes, prepared with 5% (w/v) ethanol. Bottles were sealed with foil-lined caps and stored at room temperature in the dark. A positive control (LAS Reference # 1 Dodecene-1) was prepared similarly and used to verify the biological activity. Periodically, chemical analyses were made by sacrificing a bottle with PNCB and a control. A 25 mL aliquot of hexane was injected into the bottle, the bottle vigorously shaken, and the phases allowed to separate. A portion of the hexane was collected, transferred to a 2 mL cell, and the UV absorption determined. Recoveries of spiked samples for PNCB were 97.6%.	
Result	:	Losses from the distilled water control were insignificant (PNCB concentration of 1.008 mg/L at day 0 and 0.996 mg/L at day 56). PNCB concentration at day 0 was 0.992 mg/L and dropped to 0.859 mg/L at day 56 (a 13.4% loss due to biodegradation in 56 days).	
Test substance	:	PNCB presumably as commercial grade with purity > 99%.	
Reliability	:	(2) valid with restrictions Supplemental information for this Biodegradation HPV endpoint.	
06.12.2002			(11)

3. Environmental Fate and Pathways

Id 100-00-5
Date 09.12.2002

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: static
Species	: <i>Salmo gairdneri</i> (Fish, estuary, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: no
NOEC	: = 1.8 -
LC50	: = 6 -
Method	: other
Year	: 1980
GLP	: yes
Test substance	: other TS
Method	: Employed EPA methodology 660/3-75-009. Ten fish (ave. weight of 0.97 g and mean length of 40 mm), obtained from Trout Lodge, McMillin, WA, USA were tested in one of 5 test concentrations for up to 96-h. PNCB was administered in an acetone solution at concentrations of 1, 1.8, 3.2, 5.6 and 10 mg/L plus untreated and solvent control. Antimycin A was used as a positive control. Temperature was maintained at 12 +/- 1 deg. C. Tests were conducted in soft reconstituted deionized water, supplemented with 48 mg NaHCO ₃ , 30 mg CaSO ₄ , 30 mg MgSO ₄ and 2 mg KCL per liter. Fish were unfed 48 hr prior to testing and through the experimental period. Tests were conducted in 20-L glass vessels containing 15-L of solution. Dissolved oxygen was monitored to ensure the concentration did not fall below 2 mg/L before the end of the test. Water quality parameters such as pH, ammonia, and temperature were measured; no significant changes were observed during the test for these parameters. Estimation of LC50 and 95%CI were determined using EPA statistical procedures (probit analysis).
Result	: The 96-h LC50 (95%CL) = 6.0 (4.8-7.6) mg/L.; the 48-h LC50 (95%CL) = 7.5 (6.1-9.2) mg/L; the 24-h LC50 (95% CL) = 8.8 (no CL calc.) mg/L. No deaths were observed up to 3.2 mg/L through 96 hrs. At the 5.6 mg/L level the following % mortality was reported at 24, 48 and 96-h: 0%, 10%, 50%. At 10 mg/L, mortality reached 70%, 90%, and 90% at 24, 48 and 96-h. Toxicity as exhibited by surfacing was seen at concentrations of 3.2 mg/L and higher beginning 24 hr after treatment while loss of equilibrium also was seen at 10 mg/L at all three time points. Dissolved oxygen ranged between 9.2-7.1 mg/L, pH between 7.2-7.6 and total nitrogen (NH ₃) of <0.1 - 0.3 mg/L.
Test substance	: PNCB with purity of > 99%.
Reliability	: (2) valid with restrictions Well documented study which followed regulatory guidance for study conduct. LC50 value identical to that reported for guppies (Deneer et al. 1987. Aquat Toxicol 10:115) and similar to LC50 of 8.3 for bluegill sunfish (Solutia study no. AB-80-316)
Flag	: Critical study for SIDS endpoint
06.12.2002	

(12)

Type	: other
Species	: other
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	:
LC50	: = 50.2 -
Method	: other
Year	: 2002
GLP	:
Test substance	: other TS
Method	: An acute freshwater fish 96-h LC50 was calculated using ECOSAR, from

the US EPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.

Test substance : p-Nitrochlorobenzene.

Reliability : (2) valid with restrictions
Supplementary information.

25.11.2002 (21)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static

Species : *Daphnia magna* (Crustacea)

Exposure period : 48 hour(s)

Unit : mg/l

Analytical monitoring : no

NOEC : = 3.2 -

EC50 : = 10 -

Method : other

Year : 1980

GLP : yes

Test substance : other TS

Method : Employed EPA methodology 660/3-75-009. Ten < 24-h old *D. magna* Straus (lab culture) were tested at 23 deg C in a series of three replicates per test concentration. PNCB in dimethyl formamide was tested at 6.25, 12.5, 25, 50 and 100 mg/L plus untreated control and solvent control. Morbidity and mortality were checked daily. Tests were conducted in 250-mL beakers containing 200 mL of solution. Well water from St Peter, MO, USA was used. Daphnids received no food 48-h prior to treatment. Water quality was measured to record dissolved oxygen, pH, alkalinity, hardness and temperature. Determination of EC50 and 95%CL were made using EPA statistical procedures (Steven, CE 1976. ASTM STP 634).

Result : 48-h EC50 (95% CL) = 11.1 mg/L (8.9-13.3); 24-h EC50 = 18.8 (16.9-21.1) mg/L. Dissolved oxygen ranged between 8.1 -8.4 mg/L, pH was 7.0-8.1, alkalinity was 266-340 mg/L and hardness ranged between 226-318 mg/L. Temperature remained constant at 23 deg. C. The NOEC was < 6.25 mg/L. Per cent deaths seen at 24 and 48 hr respectively were : none in control or solvent control, 6.25 mg/L - 3%, 23%; 12.5 mg/L - 7%, 50%, 25 mg/L - 83%, 90%, 50 mg/L - 100% at both time points and at 100 mg/L - 100% deaths at both time points.

Test substance : PNCB with purity of > 99%.

Reliability : (2) valid with restrictions Well conducted study following regulatory accepted test guidelines. Solutia study (AB-80-317) using similar design and employing two replicates per dose resulted in 48-h EC50 of 10 (9-12) mg/L. Well conducted study following regulatory accepted test guidelines. Solutia study (AB-80-317) using similar design and employing two replicates per dose resulted in 48-h EC50 of 10 (9-12) mg/L.

Flag : Critical study for SIDS endpoint

06.12.2002 (19)

Type : other

Species : *Daphnia magna* (Crustacea)

Exposure period : 48 hour(s)

Unit : mg/l

Analytical monitoring : no

EC50 : = 55.3 -

Method : other

Year : 2002

GLP : yes

Test substance : other TS

4. Ecotoxicity

Id 100-00-5

Date 09.12.2002

Method	: Calculated an acute Daphnid 48-h EC50 employing ECOSAR from US EPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.	
Test substance	: p-Nitrochlorobenzene	
Reliability	: (2) valid with restrictions	Supplementary information.
	Supplementary information.	
25.11.2002		(21)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	: Scenedesmus subspicatus (Algae)	
Endpoint	: biomass	
Exposure period	: 48 hour(s)	
Unit	: mg/l	
Analytical monitoring	:	
EC10	: = 2.2 -	
EC50	: = 8 -	
growth EC10	: = 4.9 -	
growth EC50	: = 16 -	
Method	: other	
Year	: 1986	
GLP	: no data	
Test substance	: other TS	
Method	: DIN 38412, Part 9 - The green alga <i>S. subspicatus</i> (Strain 8681 SAG) was used to conduct a modified cell multiplication inhibition test. A stock solution of the test substance was prepared in double-distilled water and diluted to prepare a series of test concentrations ranging from 0.80-100 mg/L. The test was conducted in capped 250 ml Erlenmeyer flasks. Eight (8) replicates of each concentration were tested. Flasks were inoculated with the cell suspension (cell concentration of 10E5 cells/ml in each flask), placed on a white surface, protected from sunlight, shaken daily, and exposed to constant artificial lighting. The temperature was maintained at 24 +/- 1 deg C. and the relative humidity was 50%. A control group (8 replicates) was tested concurrently. On each measurement day, 50 ml were collected from each of two flasks from each test concentration or the control. The extinction value of the monochromatic radiation (578 nm wavelength) of the cell suspension was determined for each test concentration and the control. Samples were collected and measurements were made at the beginning of the test and after 24 and 48 hrs. Biomass determination was based on measurement of optical density (turbidity). EC values were determined by regression analysis.	
Result	: Mean measured values of control group at 48 hrs were extinction value - 0.068; Biomass - 3.6 x 10E5 cells/ml. Results of the cell multiplication inhibition test of PNCB were: 48-h Biomass EC10 = 2.2 mg/L; 48-h Biomass EC50 = 8.0 mg/L. The 48-h average specific growth rate EC10 = 4.9 mg/l; 48-h average specific growth rate EC50 = 16 mg/L.	
Test substance	: pNCB, purity unspecified.	
Reliability	: (2) valid with restrictions	
	Small deviations from standard study design, including shorter duration used (48 vs 72 h), and limited information presented on each test concentration at each measurement point.	
Flag	: Critical study for SIDS endpoint	
06.12.2002		(5)
Species	: other algae	
Endpoint	:	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
Analytical monitoring	:	

4. Ecotoxicity

Id 100-00-5

Date 09.12.2002

EC50	:	c = 35.3 -	
Method	:	An acute green algal 96-h EC50 was calculated using ECOSAR, from the USEPA. The SAR for esters was used. The structure was determined from the CAS RN, as stored in the accompanying database of SMILES notations within ECOSAR.	
Test substance	:	p-Nitrochlorobenzene.	
Reliability	:	(2) valid with restrictions	
		Supplementary information.	
25.11.2002			(21)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	: LD50
Species	: rat
Strain	: Sprague-Dawley
Sex	: male/female
Number of animals	: 20
Vehicle	: other
Value	: 530 - mg/kg bw
Method	: other
Year	: 1975
GLP	: no
Test substance	: other TS
Method	: Methodology similar to OECD # 401, except with fewer animals; PNCB was administered by gavage in 10% corn oil to groups of 5 mixed sex SD rats at dosages of 398, 501, 631 and 794 mg/kg. Animals were observed for signs of toxicity and death daily for 14 days. Body weights were recorded on study day 0 and weekly thereafter. Animals dying and all survivors to d14 were necropsied. Food and water were given ad libitum and temp., humidity and light were controlled. LD50 and CI were calculated by the method of deBeer, J. Pharmacol Experiment Ther 86:1.
Result	: LD50=530 mg/kg with CI of 480-590 mg/kg; Incidence of deaths observed at each dose group were: 1/5 @ 398 mg/kg, 2/5 @ 501 mg/kg, 4/5 @ 631 mg/kg, and 5/5 @ 794 mg/kg. Deaths occurred during study days 1-5, with most occurring during days 1-3. Clinical signs of toxicity observed included: increased weakness, slight tremors, ocular discharge. Necropsy of the viscera in decedents resulted in identification of lung hyperemia and discoloration of the liver, spleen and kidneys. Viscera of survivors (14 days) appeared normal.
Test substance	: No data; assumed to be commercial grade with purity > 99%.
Reliability	: (2) valid with restrictions Study conducted prior to codification of OECD guideline 401 or inception of US GLPs (1979). Fewer animals used than stipulated in 401. Test results are highly consistent with 17 other rat OLD50 values ranging between 294-830 mg/kg as found in the ECB IUCLID PNCB, 2000.
Flag	: Critical study for SIDS endpoint
06.12.2002	(20)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	: rat
Sex	: male/female
Strain	: Fischer 344
Route of admin.	: inhalation
Exposure period	: 6 hr/day
Frequency of treatment	: 5 days per week for 13 weeks
Post obs. period	:
Doses	: 0, 1.5, 3, 6, 12 and 24 ppm
Control group	: yes
NOAEL	: < 1.5 - ppm
LOAEL	: = 1.5 - ppm
Method	: OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	: 1989
GLP	: yes
Test substance	: other TS
Method	: Groups of 10 male and 10 female F-344 rats were exposed in whole body stainless steel and glass chambers to vapors containing 0, 1.5, 3, 6, 12 or 24 ppm PNCB for 6 hr/d, 5 days per week, for 13 weeks. Vapor was generated by transfer of bulk PNCB into a flask and attached to a vapor generator with a rotary evaporation system. The resulting vapor was forced into a condenser and temperature maintained by circulating oil. Generator output and flow were automatically controlled. Chamber monitoring was performed using a GC/EC system. Low volatility of PNCB limited the maximum exposure vapor concentrations to the top level used in this study. Animals were individually caged, food and water administered ad libitum, and a 12 hr light:dark cycle employed. All animals were assessed for morbidity and mortality daily and weekly examined for clinical toxicity and recording of body weights. At termination of the study (13 weeks) all animals were necropsied and a full set of over 40 tissues and organs were examined microscopically for all high dose and control animals; target organs were examined for animals from lower dose groups. Organ weights and relative weights were assessed for all animals after 13 weeks of testing and included the following organs: heart, kidney, lung, liver, spleen, testis and thymus. The following hematology parameters were assessed on study day 1 (Methemoglobin only), 4, 23, and at 13 weeks from all rats from each study group: HCT, HGB, RBC, RETIC, MCV, MCH, MCHC, PLAT, WBC, MET, and WBC differentials. Similarly, the following clinical chemistry parameters were measured from all rats at similar time points as hematology: BUN, CREAT, TPROT, ALB, GLOB, ALT, AP, CK, SDH, and bile acids. Williams parametric multiple comparison procedure was employed to statistically assess group-wise comparison of organ and body weights. Shirley's test for nonparametric analysis was used for clinical chemistry and hematology assessments. $P < 0.05$ and < 0.01 were used in all cases.
Remark	: Sperm morphology and vaginal cytology evaluations were performed on rats exposed to 0, 6, 12, or 24 ppm PNCB. Male rats exposed to 24 ppm exhibited significantly lower left epididymal, cauda epididymal, and testis weights and lower spermatid heads/testis, spermatid counts and spermatozoal concentrations than control rats; estrous cycle length was decreased in all groups of PNCB-exposed females.
Result	: Mean concentrations in all test chambers were between 99-100% of target concentrations. No treatment related deaths, obvious clinical signs of toxicity, or effects on body weight were observed at any dose level. Hematology findings were consistent with methemoglobinemia and macrocytic (increased MCV) and hyperchromic (MCHC increase) hemolytic anemia seen at all test levels. Compensatory hematopoietic cell proliferation was present and considerable hemosiderin deposition observed microscopically, and produced a pattern of effects observed with other MET-forming agents. Following are the various statistically

	<p>other MET-forming agents. Following are the various statistically elevated/depressed effects noted at each dose level: At 1.5 ppm = increased MET, normocytic RBC (F only) and decreases in HCT, HGB, RBC, ALT (M only), renal hyaline droplet formation (males only), splenic congestion and hemosiderosis; at 3 ppm = increased MET, RETIC, normocytic RBC and bile acids (M only), and decreases in HCT, HGB, RBC, ALT, (M only), AP (F only), marked increase in spleen wt and mild liver wt (F only), renal hyaline droplets (M only), bone marrow hematopoietic cell proliferation, Hardarian gland inflammation, congestion and hemosiderosis of the spleen along with hematopoietic cell proliferation and capsular fibrosis and hemosiderosis of the liver Kupfer cells (F only); at 6 ppm = increases in RETIC, MET, n-RBC, bile acids (M only), SDH (F only), MVC, spleen and liver weights and decreases in HCT, RBC, ALT, AP, TPROT, GLOB, and renal hyaline droplet formation (M only), bone marrow and splenic hematopoietic cell proliferation, Hardarian gland inflammation, splenic congestion, hemosiderosis and capsular fibrosis of the liver; at 12 ppm = decreases in HCT, HGB, RBC, AP, GLOB, ALT, TPROT and increases in MET, RETIC, n-RBC, SDH and bile acids, marked increases in spleen weights and mild increases in liver, heart and thymus weights, renal hyaline droplet formation (M only), bone marrow and splenic hematopoietic cell proliferation, Hardarian gland cell proliferation, splenic congestion, hemosiderosis, and capsular fibrosis and hemosiderosis and histiocytic hyperplasia of the liver; at 24 ppm = increases in MET, RETIC, MCV, n-RBC, HGB, SDH, bile acids and decreases in HCT, HGB, RBC, AP, GLOB, ALT, TPROT, organ weight increases of the spleen, liver, heart, thymus and decreased testes weight, renal hyaline droplet formation (M only), bone marrow and splenic hematopoietic cell proliferation, Hardarian cell proliferation, splenic congestion and capsular fibrosis, hemosiderosis of the spleen and liver, histiocytic liver hyperplasia and testicular atrophy</p>
Test substance	: PNCB determined to be > 97 % pure.
Reliability	: (1) valid without restriction
Flag	: Well documented study consistent with OECD test guideline 413
06.12.2002	: Critical study for SIDS endpoint
	(10)
Species	: rat
Sex	: male/female
Strain	: Sprague-Dawley
Route of admin.	: inhalation
Exposure period	: 6 hr/day
Frequency of treatment	: 5 days/week for 4 weeks
Post obs. period	:
Doses	: 0, 5, 15, and 45 mg/m ³ (equivalent to 0.78, 2.3 and 7 ppm)
Control group	: yes
NOAEL	: < 5 - mg/m ³
LOAEL	: = 5 - mg/m ³
Method	: OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year	: 1982
GLP	: yes
Test substance	: other TS
Method	: Groups of 10 male and 10 female SD rats were exposed via whole body in stainless steel and glass inhalation chambers to airborne concentrations of 0, 5, 15 or 45 mg/m ³ PNCB for 6 hr/day, 5 days/week for 4 weeks. PNCB was mixed with a solvent and fed into a spray atomizer through which dry air was passed. Test material flow into test chambers was controlled using a fluid metering pump. Concentrations of PNCB were determined at least 3X daily using UV spectrophotometer; particle size distribution was determined throughout the study. Parameters monitored in this study included daily morbidity and mortality checks, weekly detailed clinical observations, and body weights. Hematology parameters (HGB, RBC, HCT, RETIC, MET, clotting time, RBC morph. and total and differential

	<p>HCT, RETIC, MET, clotting time, RBC morph. and total and differential leukocytes) and clinical chemistries (BUN, SGPT, AP, GLU, ALB, TPROT, GLOB, K, CL, CA, PHOS) were analyzed at day 0 and just prior to termination (MET also analyzed after 2 weeks of testing) for 10 rats/sex/group. Ophthalmoscopic exams were conducted on all rats prior to study start and at termination. Organ (brain, testes, ovaries, heart, kidneys, pituitary, liver, lungs, spleen) weights and weight ratios were recorded at terminal sacrifice for all rats on test. Microscopic examination of over 40 tissues and organs were performed on all rats from the high dose and control groups at the end of the study. Spleens of all low and mid dose animals were also examined microscopically. Gormori's stain was used to semiquantitate the degree of hemosiderosis. A Bartlett's test was performed on study data to determine the degree of equality of variances (Snedecor and Cochran) followed by Dunnet's test for parametric parameters and the Kruskal-Wallis test along with Dunn's Summed Rank test for nonparametric parameter analysis. $P < 0.05$ was used in all cases.</p>
Result	<p>: Cumulative mean analytical exposure concentrations were 5, 16 and 45 mg/m³. Particle size distribution of the generated atmospheres established that PNCB was introduced as a vapor, rather than as an aerosol. No mortalities were observed in treated groups and mean body weights of PNCB-treated animals were similar to control values. Clinical signs of toxicity observed included: cyanosis of the conjunctivae, nasal areas and entire body in all three groups, with incidence increasing with dose. Other than a dark red appearance, no ocular abnormalities related to treatment were observed. Rats at all test levels exhibited slight reductions in HGB, HCT, RBC at one or both study intervals. Animals in the mid and high dose groups also exhibited an increase in the incidence of poikilocytosis and polychromia at the interim bleeding. MET showed a dose-related increase with levels approximating 2-8X controls. An increase in leukocytes was attributed to the aberrant inclusion of reticulocytes in the automatic counting procedure for white blood cells. Small increases in GLU and reduced PHOS levels were seen in HD females only. Statistically elevated spleen and liver weights were seen in HD males and females (and rel. liver wts in mid dose females). An increased incidence of congestion, extramedullary hematopoiesis and hemosiderosis of the spleen was observed in male and female rats exposed to 45 mg/m³ and iron-positive pigmentation (hemosiderosis) in spleens of rats from the mid and low dose.</p>
Test substance	: Greater than > 99 % pure
Reliability	: (1) valid without restriction Provided as Supplemental information as a longer-term study, conducted by the same exposure route, has been selected as the Key study for this HPV Endpoint; this study meets OECD Test Guidance 412 and was conducted under GLPs.
06.12.2002	(17)
Species	: rat
Sex	: no data
Strain	: other
Route of admin.	: oral unspecified
Exposure period	: up to 7 months
Frequency of treatment	: daily
Post obs. period	:
Doses	: 110 mg/kg/d for 20 days; 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months
Control group	: yes
NOAEL	: = .0025 - mg/kg bw
Method	: other
Year	: 1967
GLP	: no data
Test substance	: other TS
Method	: Peroral treatment of 20 albino rats at 110 mg/kg for 20 days, followed by peroral administration of PNCB to groups of rats at 5, 0.025, 0.005 and 0.0025 mg/kg/d for 7 months. Measured indices reportedly included

	0.0025 mg/kg/d for 7 months. Measured indices reportedly included hematology, liver function (blood and urine) and peripheral blood pathology.
Result	: 7/20 rats treated with 110 mg/kg PNCB for 20 days died. Groups of rats treated for 7 months exhibited marked changes in peripheral blood. Methemoglobin levels were increased within the first month of testing in the HD group; elevations occurred in groups treated with 0.005 mg/kg PNCB or higher. Hemoglobin was reduced and reticulocytes, serum alkaline phosphate and urinary bilirubin were elevated along with presence of Heinz bodies in erythrocytes at dosages of 0.005 mg/kg/d and above. The NOEL was 0.0025 mg/kg/d.
Conclusion	: Comparative study using ONCB, MNCB and PNCB. Concluded that PNCB was the most toxic isomer following systemic exposure, MNCB was intermediate, and ONCB was the least systemically toxic of the three isomers tested. All isomers exhibited essentially the same pattern of toxicity.
Reliability	: (4) not assignable Supplemental information, as this report provides but a summary of results without sufficient detail to be classified higher.

06.12.2002

(2)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	: Ames test
System of testing	: Salmonella typhimurium strains TA100, TA98, TA1535, TA1537
Concentration	: 10, 4, 3, 1.5, 1.3, 1, 0.3, 0.2, 0.04, and 0.01 mg/plate
Cycotoxic conc.	: 3 mg/plate
Metabolic activation	: with and without
Result	: positive
Method	: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year	: 1979
GLP	: yes
Test substance	: other TS
Method	: Method used was plate incorporation assay based on Ames test methods consistent with OECD 471. All tests were run in duplicate and three plates were assayed at each dosage for each run both with and without metabolic activation. The S-9 liver homogenates were prepared from male SD rats and CD-1 mice given Arochlor 1254. All tester strains were obtained from Dr. B. Ames. Sterile DMSO was used as the solvent and a solvent control was employed of 20 uL/plate DMSO. Positive controls used were: 2-aminoanthracene, 9-aminoacridine, benzo(a)pyrene, NaNo ₂ and 2-nitrofluorene. A positive response was determined upon observation of a statistically significant dose-response increase in revertant colonies. Bartlett's test was used for pairwise comparison to controls and dose response determined using regression analysis for log-log straight lines; P<0.01 was used.
Result	: A definitive positive response was observed with TA1535 without metabolic activation, with some indication that TA1535 with metabolic activation was marginally positive.
Test substance	: Greater than 99% pure
Reliability	: (1) valid without restriction
Flag	: Critical study for SIDS endpoint

06.12.2002

(18)

Type	: Cytogenetic assay
System of testing	: Chinese Hamster Ovary Cell in vitro assay
Concentration	: 50 to 5000 ug/mL
Cycotoxic conc.	:
Metabolic activation	: with and without

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Result	: positive
Method	: other
Year	: 1987
GLP	: yes
Test substance	: other TS
Method	: Study conducted according to NTP study design, testing involved 3 separate tests (2 with S9 and 3 without S9 fraction added) SD male rat Arochlor 1254-induced liver homogenate was used. Cell cultures were handled to prevent photolysis of Brdu-substituted DNA. Each test consisted of concurrent solvent and positive controls and at least 3 dose levels. Cells were incubated in McCoy's 5A medium with test agent ranging between 10.5-19 hrs, colcemid added and incubated for an additional 2 hrs and harvested/processed. 100 first-division metaphase cells were scored blind from prepared slides for each dose level. Classes of aberrations were recorded and included simple, complex and other abnormalities. Statistical analysis (Armitage trend test; Margolin multiple comparison test) were conducted on both the dose-response curve and individual dose points; significance was determined as $P < 0.05$ for single data points and $P < 0.015$ for trend.
Result	: Initial trials run at harvest times of 10.5 hr w and w/o S9 were negative. A follow up trial w/o S9 conducted at a higher dose level (700, 800 and 900 ug/ml) and incubated for 19 hrs (because PNCB induced cell cycle delay in the earlier study) resulted in an increase in aberrant cells only at 900 ug/plate; A repeat of this study at levels of 500, 600 and 700 ug/plate resulted in a dose related increase only at the top dose used. Repeat of the metabolic activation trial using a longer period to harvest (19 hr) produced an increase in aberrant cells.
Reliability	: (2) valid with restrictions Provided as Supplemental information as an in vivo cytogenetics study has been used to fulfill this HPV endpoint.

07.11.2002

(9)

5.6 GENETIC TOXICITY 'IN VITRO'

Type	: Cytogenetic assay
Species	: rat
Sex	:
Strain	: Sprague-Dawley
Route of admin.	: gavage
Exposure period	: once
Doses	: 30, 100 and 300 mg/kg
Result	: negative
Method	: OECD Guide-line 475 "Genetic Toxicology: In vivo Mammalian Bone Marrow Cytogenetic Test - Chromosomal Analysis"
Year	: 1983
GLP	: yes
Test substance	: other TS
Method	: Dose levels selected based on pilot study which produced 1/4 deaths @ 400 mg/kg and 4/4 deaths @ 600 mg/kg. Five rats/sex/time period were administered PNCB in corn oil by gavage. Metaphase cells were collected from rat bone marrow (femur) at harvest times of 6, 12 and 24 hrs after treatment from 5 rats/sex. Colchicine was administered 2 hr prior to sacrifice to arrest cells in c-metaphase. Marrow was exposed to hypotonic solution and fixed, cells and slides prepared and stained. All slides were coded before reading. Positive (cyclophosphamide) and negative (corn oil) controls were used for comparative purposes. Mitotic index was calculated based on counting of at least 500 slides and all breaks, deletions, translocations and other changes recorded. Breaks or aberrations between treated vs control groups were compared by Chi-square analysis. $P < 0.05$ was used.

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Result	: Rats dosed with 100 and 300 mg/kg PNCB exhibited signs of cyanosis; animals given 300 mg/kg lost weight between time of dosing and sacrifice. No significant differences were observed in the frequency of breaks or aberrations between PNCB-treated and control groups at any of the three time points measured.
Test substance	: Test material purity of > 99%.
Reliability	: (2) valid with restrictions Time points measured did not include a period beyond 24 hr, but sufficient cells in metaphase were obtained at this time point that it was determined that there was no need to extend the sampling period.
Flag 04.12.2002	: Critical study for SIDS endpoint

(13)

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	: Two generation study
Species	: rat
Sex	: male/female
Strain	: Sprague-Dawley
Route of admin.	: gavage
Exposure period	: F0 & F1 Adults-premating through litter weaning (Fo) and postweaning (F1)
Frequency of treatment	: daily (7d/wk) gavage
Premating exposure period	
Male	: FO- 14 weeks; F1- 18 weeks
Female	: FO-14 weeks; F1 - 18 weeks
Duration of test	: FO M/F - 167d; F1 M/F- 219d
Doses	: 0, 0.1, 0.7 and 5.0 mg/kg/day
Control group	: yes, concurrent vehicle
NOAEL Parental	: = 5 - mg/kg bw
NOAEL F1 Offspr.	: = 5 - mg/kg bw
NOAEL F2 Offspr.	: = 5 - mg/kg bw
Method	: OECD Guide-line 416 "Two-generation Reproduction Toxicity Study"
Year	: 1984
GLP	: yes
Test substance	: other TS
Method	: Test material was administered to groups of 15M and 30F rats (vehicle control group also included) in corn oil to F0 and F1 generations during a premating (14 wks for F0 and 18 wks for F1) growth period, and through the ensuing mating, gestation and lactation intervals (1 litter/generation). F1 rats continued on treatment during a post-weaning period of 30d. Dosing concentrations analyzed by GC weekly for the first week of the study and monthly thereafter for accuracy. Body weights were recorded weekly for F0 and F1M. For F0 and F1 F wts were recorded weekly through the growth period and up to mating, then resumed after mating until sacrifice. Food consumption was recorded weekly for F0 and F1 M from study start up to mating, then resumed after mating through study term. Food consumption for adult females F0 and F1 was recorded weekly through the growth period and again after weaning of litters. Cageside observations for morbidity and mortality were made weekly, as well as daily observations of clinical signs. Temperature, humidity and light-dark cycles were controlled. F0 adults were sacrificed following weaning of the F1 litters and given a gross postmortem examination; reproductive tissues (testes, epididymides, seminal vesicles) were evaluated histopathologically for all control and high dose males. Adult F1 M and F rats were sacrificed

following completion of a post-weaning treatment interval, given a gross necropsy. A full histopathological examination of over 40 tissues and organs (including gonads) was performed on 10 randomly selected F1 adult animals/sex/group. Pups delivered to F0 and F1 females were evaluated for growth, survival and external irregularities during lactation days 0, 4, 14 and 21. F1 pups not selected for the adult generation were sacrificed and given a gross postmortem exam. Tissues were evaluated histopathologically (~40 tissues/organs) from 5/sex/group of F1 weanlings and F2 weanlings. Body weights and changes, food consumption, gestation length and number of offspring were analyzed using ANOVA techniques followed by Dunnett's Test for parametric parameters and Kruskal-Willis test followed by Dunn's Rank Sum for nonparametric analysis. Mortality and pregnancy rates, fetal and mating indices and pup survival were analyzed using Chi-square, followed by Fisher Exact test and Armitage's test for linear trend. The level of significance was reported at both the 5% and 1% levels.

Remark : Slight decreases in male and female fertility indices, as well as testicular effects seen in 3 HD male rats in the FO generation are considered spurious findings, unrelated to treatment. No such effects were noted in the F1 generation, which were exposed over a considerably longer dosing period. Likewise, no testicular effects were observed in a group of 50 male rats exposed to 5 mg/kg/d PNCB by gavage for 24 months, a dosing regimen similarly used here, albeit for substantively longer than the 14 weeks rats in the HD group in this study were dosed.

Result : Dosing solutions were confirmed analytically as accurately prepared. No treatment-related mortalities could be affirmed in this study, although several gavage-related deaths occurred sporadically. Mean body weights and weight gains of all FO male groups were similar; FO females exhibited slightly, but not statistically lower, body weights at all treatment levels. This finding was considered unrelated to treatment as there was no dose-response effect noted. Food consumption values were similar between treated and control FO males and females, except for HD females which consumed slightly, but not statistically significantly, more food through the first 6 weeks of the study. The mating index (no. mating/total given opportunity to mate) were similar for all FO Males. The mating index for FO Females was 86.7, 80, 71.4 and 71.4%, respectively, from control through HD group; as all these values were within the historical control range for this index in this laboratory, these findings were considered unrelated to treatment. No statistical differences were seen in either pregnancy rate or male fertility index between PNCB-treated and control animals from the FO generation. Three HD male rats in the FO parental generation were found to have testicular degeneration upon microscopic examination. FO dams treated with PNCB during gestation and lactation exhibited mean body weights and length of gestation indices comparable to control levels. The number of live and dead pups at birth and pup weights during lactation of pups from FO dams were unaffected by PNCB dosing. Pup survival in the HD group was slightly, but statistically significantly lower than the control group. This finding was related to the complete loss of two litters in this group, a phenomenon experienced within the test lab on an infrequent, but not unusual, basis. Thus, this finding was judged unrelated to PNCB treatment. No compound-related gross postmortem changes were observed in the FO adults or F1 weanlings. F1 generation: No treatment-related effects were seen in any test group for survival, mean body weights and gains, and food consumption during mating, gestation and lactation. No treatment-related effects were observed during the gross postmortem evaluation of F1 adults. An increase in extramedullary hematopoiesis and brown pigmentation of reticuloendothelial cells of both sexes of the HD treated groups were observed following histological examination of F1 animals. All three PNCB-treated groups of F1 females exhibited a slightly (but not statistically) lower mating index than the control group; however, no dose-response was evident and the number of pregnant females in all groups, control and treated, were similar. Thus, this observation was not considered treatment-related. Male (FO1) mating and

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	<p>observation was not considered treatment-related. Male (FO1) mating and fertility indices were unaffected by treatment. Litter and pup survival indices in groups of F2 generation animals were comparable between all treated and control groups. Similarly, pup weights were unaffected by treatment at all test levels. No evidence of toxicity was observed during the gross postmortem evaluation of F2 pups and no compound-related changes were observed during histological examination of tissues in F1 and F2 weanling pups.</p>	
Test substance	: ONCB with purity of 99.43%	
Reliability	: (1) valid without restriction	
	Well documented GLP study meeting OECD Test Guideline 416.	
Flag	: Critical study for SIDS endpoint	
04.12.2002		(15)
Type	: other	
Species	: mouse	
Sex	: male/female	
Strain	: B6C3F1	
Route of admin.	: gavage	
Exposure period	: 105 days	
Frequency of treatment	: daily, 7 days per week for 7 days prior to cohousing and 98 days of cohousing	
Premating exposure period		
Male	: 7 days	
Female	: 7 days	
Duration of test	: 98 days of continuous breeding	
Doses	: 0, 62.5, 125 and 250 mg/kg/d	
Control group	: yes, concurrent vehicle	
Method	: other	
Year	: 1993	
GLP	: yes	
Test substance	: other TS	
Method	: Standard Continuous breeding protocol designed by NTP and published as Lamb, 1985. J. Amer. Coll. Toxicol. 4:163-171. Based on 2 week toxicity test to establish dose levels, animals are individually housed for 7 days, then cohoused in breeding pairs for 98 days, and allowed to propagate. During this period the following indices are recorded: clinical signs of toxicity, mortality, parental body weight and average consumption of water during representative weeks, fertility (e.g. no. of pairs producing a litter/number of breeding pairs), the no. of litters per pair, the no. live pups/litter, % pups born alive, sex ration of pups and pup body weights after birth). The last litter born during the holding period (5 weeks) following the breeding period is reared until weaning after which treatment of the F1 animals was initiated and these animals used for assessment of second generation fertility. For this phase, siblings were cohoused until sexual maturity, when 20 non-sibling males and females per treatment group were cohoused for 7 days and then housed singly through delivery. Endpoints for this mating trial were the same as for the F0 generation. At termination of F0 and F1 generations, animals were necropsied and evaluations made for organ weights (ovaries or testes and epididymides from 5 per group, control and HD), body weights, epididymal sperm motility, sperm morphology, sperm count and estrual cyclicity. Methemoglobin measurements and spleen weights were recorded for both the F0 and F1 generations. Proportional data were assessed statistically using the Armitage trend test, with each dose group compared to control using a chi-square analysis. Absolute body and organ weights were compared using Shirley's or Dunns test while dose related trends were identified by Jonckheere's test. Vaginal cytology was analyzed using an analysis of variance described by Morrison to test for simultaneous equality. A p value of <0.05 or <0.01 was used.	
Result	: Fertility of mice dosed with PNCB decreased progressively with the duration of dosing and with increasing dose and being statistically different	

duration of dosing and with increasing dose and being statistically different from controls at the high dose level. Most mice exposed to 250 mg/kg were cyanotic. Spleen and liver weights of F1 PNCB-treated mice reportedly were significantly greater than those of the controls. Survival and body weights of F1 (final litter) and F2 pups were significantly decreased at 250 mg/kg and at 125 mg/kg (F1 only).

Test substance : pNCB with purity of 97%

Reliability : (1) valid without restriction
GLP study, peer reviewed and followed an established study design.
Submitted as Supplemental information as a previously listed rat 2-generation reproduction study fulfills this HPV endpoint.

06.12.2002

(10)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat

Sex : female

Strain : Sprague-Dawley

Route of admin. : gavage

Exposure period : once per day

Frequency of treatment : gestation days 6 through 19

Duration of test : rats sacrificed on gestation day 20

Doses : 5, 15 and 45 mg/kg/day

Control group : yes

NOAEL Maternalt. : < 5 - mg/kg bw

NOAEL Teratogen : = 15 - mg/kg bw

NOAEL Fetotoxicity : = 15 - mg/kg bw

Method : OECD Guide-line 414 "Teratogenicity"

Year : 1980

GLP : yes

Test substance : other TS

Method : Groups of 24 mated female rats were dosed daily by gavage (test material dissolved/suspended in corn oil) during gestation days 6-19. All rats were observed for mortality and abnormal behavior twice daily from gestation day 0 through day 20, at which time all animals were sacrificed and maternal spleen weights recorded. Detailed physical exams for signs of toxicity were recorded on study days 0, 6, 10, 15 and 20. Maternal body weights were recorded at several intervals throughout the study. At sacrifice the uterine horns were examined for implantation sites, resorptions and the number of viable or non-viable fetuses. The number of corpora lutea were also recorded. The sex and weights of all live fetuses were recorded and all fetuses were examined for external abnormalities. One-half of the fetuses per litter were examined for skeletal malformations while the other half were examined for internal anomalies. The following statistical analyses were performed: For interval data (body wts, wt changes, reproductive data) Bartlett's test was used to determine equality of variance and ANOVA and Dunnett's test used for parametric data while the Kruskal-Wallis test and Summed Rank test used for nonparametric data (Snedecor and Cochran). For Incidence data, i.e. mortality rates, % and incidence of variations and malformations comparisons were made using the Chi-square contingency table and the 2X2 Fisher Exact test employing the Bonferroni inequality estimate; linear trend was evaluated using the Armitage test. Comparisons were made using the litter as the comparative entity. Both the 5% and 10% level of statistical significance were reported for each parameter.

Result : Maternal toxicity (reduced body weight gain during the treatment period and increased spleen weights), fetotoxicity (increased no. resorptions/litter), embryotoxicity (increased no. fetuses with unossified sternebrae, incompletely ossified cervical and vertebral transverse

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processes) and fetal skeletal (predominantly angulated ribs) malformations were observed at the 45 mg/kg dosage level. At 15 mg/kg, similar maternal toxicity but no fetotoxic/embryotoxic or teratogenic responses were observed. At 5 mg/kg, only a slight increase in spleen weight was observed in maternal animals.

Test substance : purity > 99%.

Conclusion : PNCB produced teratogenic effects only at dosages which produced significant maternal toxicity.

Reliability : (1) valid without restriction
Provided as Supplemental information as a 2-Generation Reproduction study has been used as the Key study to fulfill the Reproductive Toxicity HPV Endpoint. This study meets OECD Test Guideline 414 and was conducted under GLPs.

06.12.2002

(14)

Species : rabbit

Sex : female

Strain : New Zealand white

Route of admin. : gavage

Exposure period : gestation days 7 through 19

Frequency of treatment : once daily

Duration of test : animals sacrificed on gestation day 30

Doses : 0, 5, 15, 40 mg/kg

Control group : yes, concurrent vehicle

NOAEL Maternalt. : = 15 -

NOAEL Teratogen : = 15 -

Method : OECD Guide-line 414 "Teratogenicity"

Year : 1980

GLP : yes

Test substance : other TS

Method : Groups of 18 mated female NZ white rabbits were administered PNCB in corn oil (constant volume of 2 ml/kg) in corn oil at PNCB concentrations of 0 (vehicle control), 5, 15, and 40 mg/kg on gestation days 7 -19. Animals were evaluated for detailed signs of toxicity on test days 0, 7, 10, 15, 19 and 30; body weights were recorded on test days 0, 7, 19 and 30. Daily observations were made for morbidity and mortality. Food and water were administered ad libitum and a 12 light:dark cycle was employed. Temperature and humidity were controlled. All animals were examined externally and 1/2 were evaluated for soft tissue malformations and the other 1/2 for skeletal findings. The following statistical analyses were performed: For interval data (body wts, wt changes, reproductive data) Bartlett's test was used to determine equality of variance and ANOVA and Dunnett's test used for parametric data while the Kruskal-Wallis test and Summed Rank test used for nonparametric data (Snedecor and Cochran). For Incidence data, i.e. mortality rates, % and incidence of variations and malformations comparisons were made using the Chi-square contingency table and the 2X2 Fisher Exact test employing the Bonferroni inequality estimate; linear trend was evaluated using the Armitage test. Comparisons were made using the litter as the comparative entity. Both the 5% and 10% level of statistical significance were reported for each parameter.

Result : Mortality so high at 40 mg/kg level that this study group was terminated without additional data collection. 15 mg/kg and 5 mg/kg- no effects on survival or maternal body wts, no treatment-related effects in uterine implantation data, fetal wts or sexing data. No statistically significant differences seen in skeletal malformations between treated and control groups nor was there any treatment-related increase in the incidence of external or soft tissue findings.

Test substance : PNCB > 99% pure.

Reliability : (1) valid without restriction
Well conducted study following GLP guidance and OECD study design. Limited due to excessive no. of deaths at the high dose group which disallowed any developmental toxicity information to be obtained from this

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disallowed any developmental toxicity information to be obtained from this study group. Supplemental information, as a 2-Generation Rat Reproduction study has been used to fulfill the Reproductive Toxicity HPV Endpoint

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5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

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7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT